STUDIES IN SALIVARY GLANDS AND THEIR SECRETIONS IN HEALTH AND DISEASE

by

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FIGURES and TABLES.

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SUMMARY

Some new methods and some established ones have been applied to studies of salivary glands in health and certain disease states.

A technique of recording the pattern of salivary flow has made it possible to collect saliva samples accurately at several different but constant flow rates. The effect of varying salivary flow rate on the parotid and submandibular concentrations of electrolytes, iodide, uric acid and also the activity of carbonic anhydrase has been demonstrated and the normal ranges defined. It is important to relate the concentration of some salivary constituents, e.g. iodide, to the plasma level.

Combined quantitative and radioisotopic methods have been used to determine basic values for the metabolism of iodine in salivary glands and saliva. Measurement of the salivary specific activity after a tracer dose has the advantage that it is independent of flow rate as the ratio of stable to radioiodine is constant at different flow rates. Normal ranges have been described for salivary iodide concentration, clearance, absolute quantities secreted in unit time and saliva/plasma ratios. The salivary iodide concentrating mechanism is normal in altered states of thyroid function and also in fibrocystic disease where previously high salivary iodide levels had been reported. In Sjögren's syndrome however low saliva/plasma ratios have been found and this suggests that the salivary iodide trap may be involved in this condition.

. The chemical nature of the salivary iodine has been studied and found to be almost entirely in the inorganic form in health and in some thyroid disease states. In contrast the urinary iodine, normally inorganic, contains organic iodinated compounds in thyrotoxicosis and in dehalogenase deficiency. Some advantages of the salivary specific activity method over the urinary method for the indirect measurement of the plasma inorganic iodine are demonstrated.

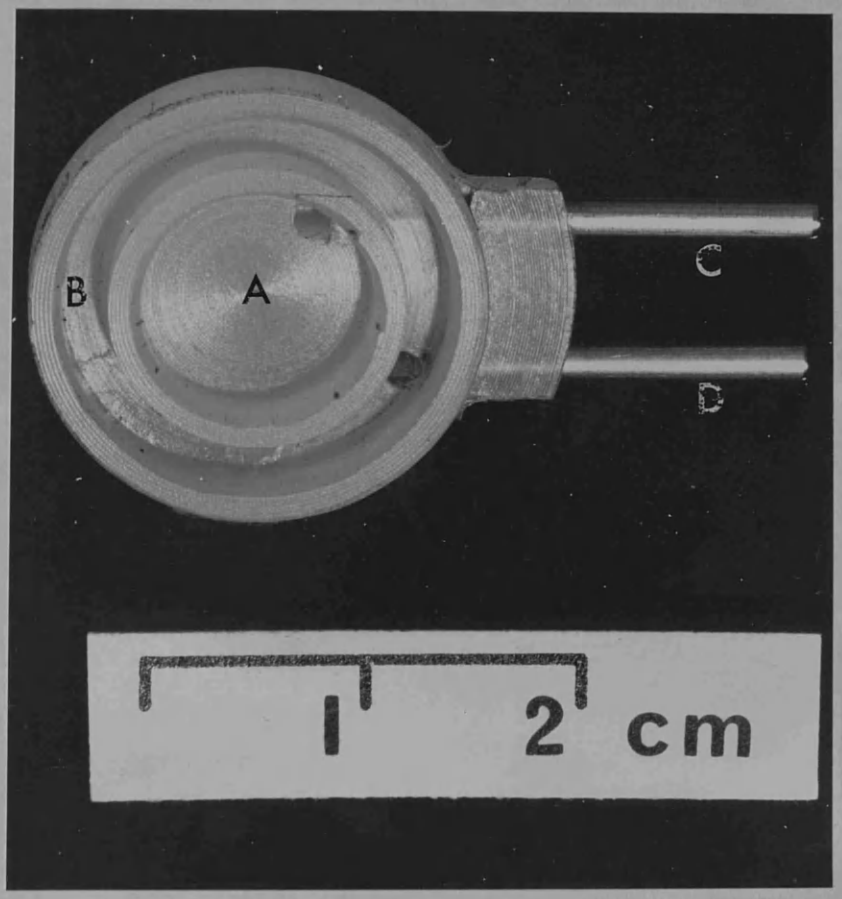
Anions of the VIIth periodic group include iodide, bromide and pertechnetate. Pertechnetate, like iodide, is concentrated in saliva. Simultaneous administration of isotopes ^{132}I and $^{99m}TcO_4$ allow direct comparison of salivary gland concentrating ability to be made on the same saliva sample thus eliminating the variable of flow rate. The isotope $^{99m}TcO_4$ has many advantages over isotopes of iodine as a clinical tracer and its use for radioisotopic visualisation of the salivary glands has been demonstrated for the first time.

The criteria for diagnosis of oral and salivary gland involvement in Sjogren's syndrome have been examined. The comparative value of tests of salivary gland function have been assesssed in 30 patients with a clinical diagnosis of Sjögren's syndrome. The advantages of the new technique of hydrostatic sialography are demonstrated. Good correlation was shown between sialographic appearances, salivary flow

rate measurements and clinical signs and symptoms. Labial gland biopsy shows a high occurrence of focal lymphocytic infiltration in patients with Sjögren's syndrome as compared with a control series. The onset of xerostomia and xeropthalmia showed no well defined relationship to the menopause. Both these components of the 'sicca syndrome' may arise together but often they commence and progress independently. While a high incidence of auto-immune thyroid disease is found in Sjögren's syndrome, an increased incidence of Sjögren's syndrome was not found in patients presenting clinically with auto-immune thyroid disease.

PART I

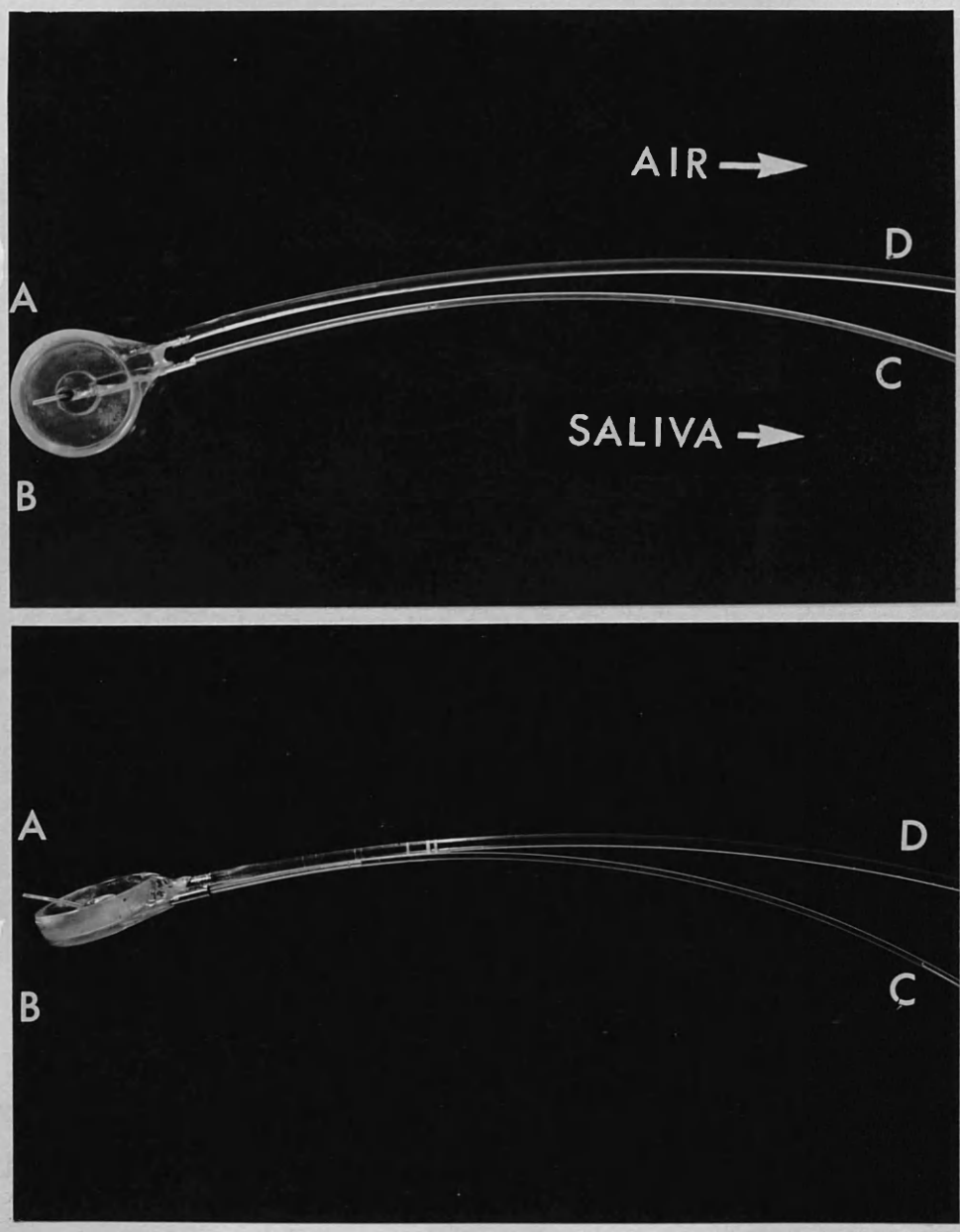
FIGURE I, 1



MODIFIED CARLSON CRITTENDEN CUP

(A) Inner Chamber
(B) Outer Chamber
(C) Tube - Saliva
(D) Tube - Air Suction

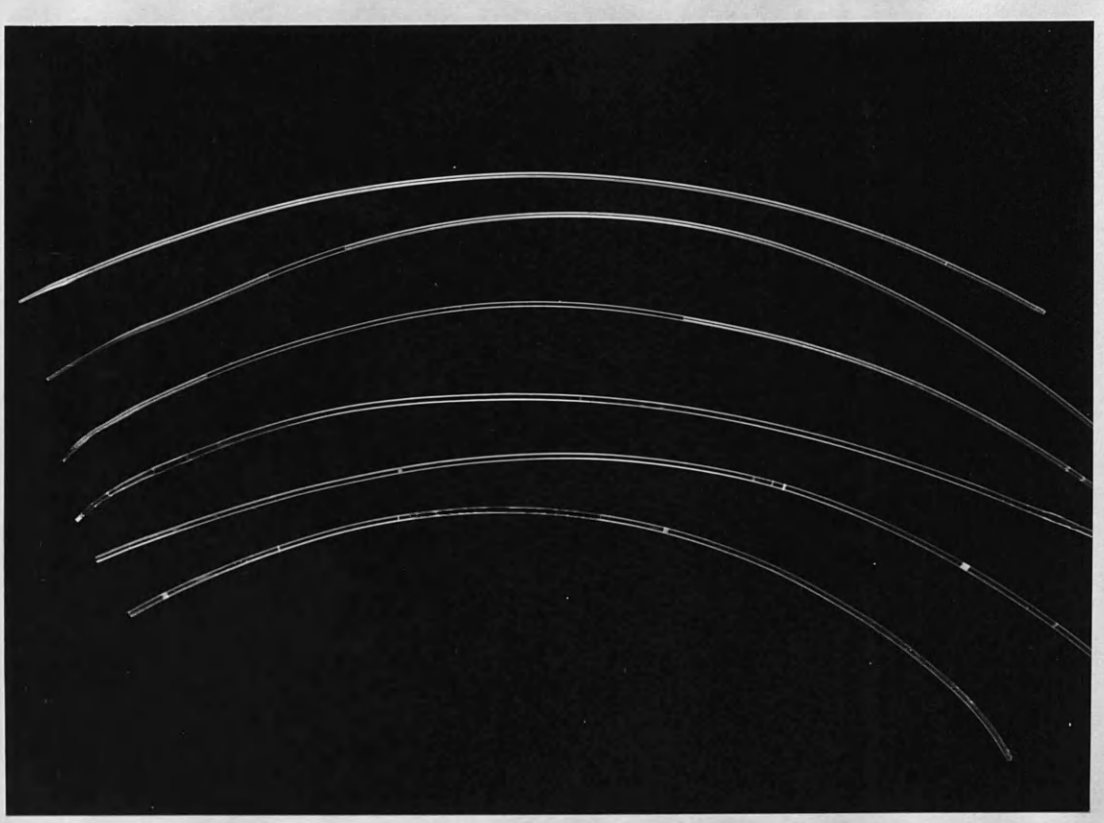
FIGURE, I, 2



KERR METHOD FOR PAROTID SALIVA COLLECTION

(A) Polyethylene catheter
(B) Suction Cup
(C) Tube - Saliva
(D) Air Suction

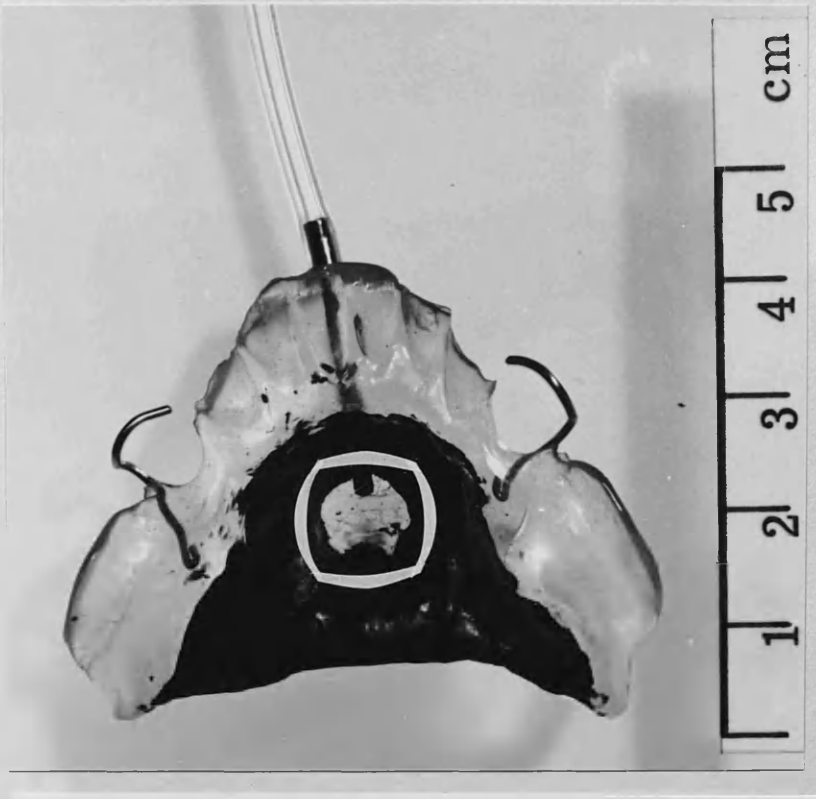
FIGURE I, 3



POLYETHYLENE CATHETERS OF VARYING SIZES TAPERED AT ONE END FOR SUBMANDIBULAR DUCT CATHETERISATION

FIGURE I, 4

A)



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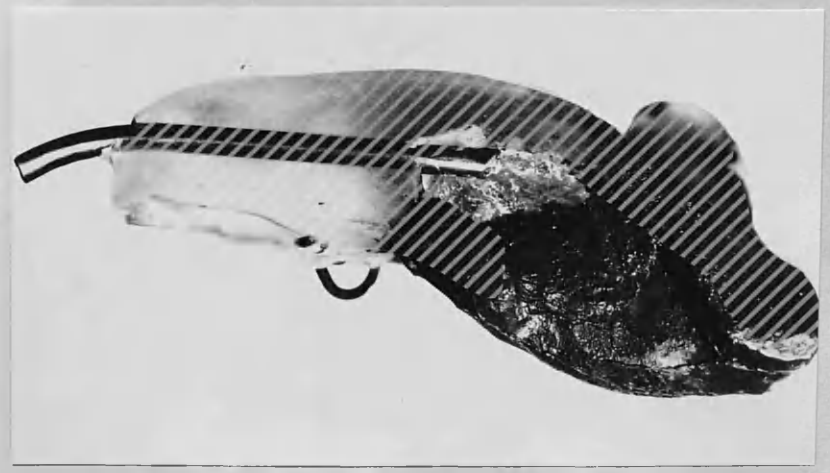
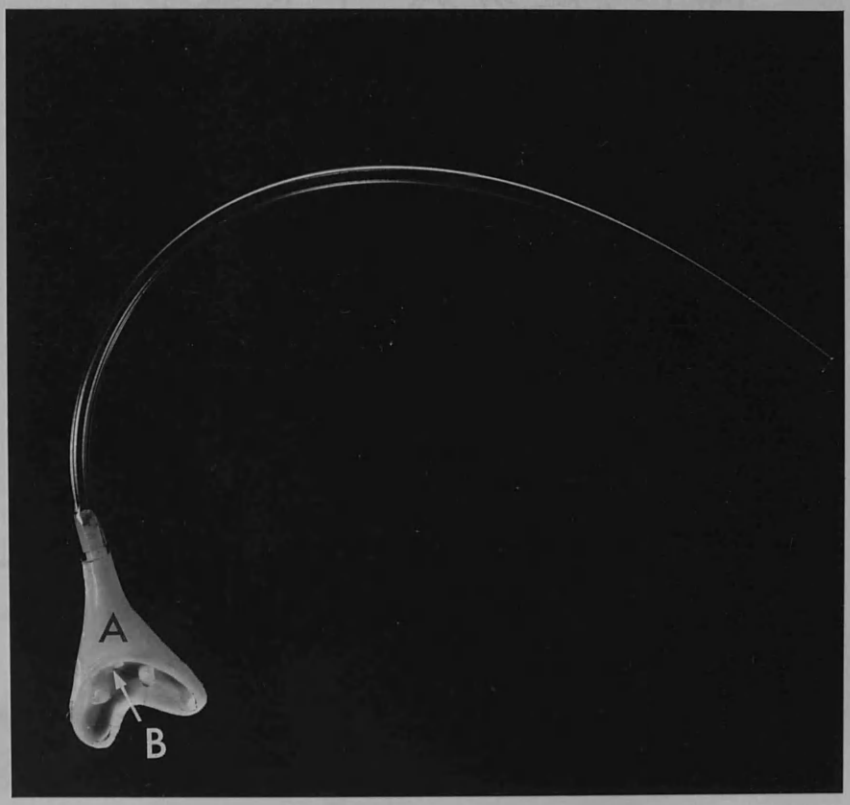


SCHNEYER SEGREGATOR FOR COLLECTION OF SUBMANDIBULAR SALIVA. THE CHAMBER (CIRCLED) IS PLACED OVER THE SUBMANDIBULAR DUCT ORIFICES

(A) Seen from below (B) Vertical cross section

FIGURE I, 5



BLOCK AND BROTTMAN SEGREGATOR METHOD OF SUBMANDIBULAR SALIVA COLLECTION.

The preformed plastic cup (A) is placed over the submandibular duct orifice at (B) and maintained in place by adding rubber base impression material.

FIGURE I, 6

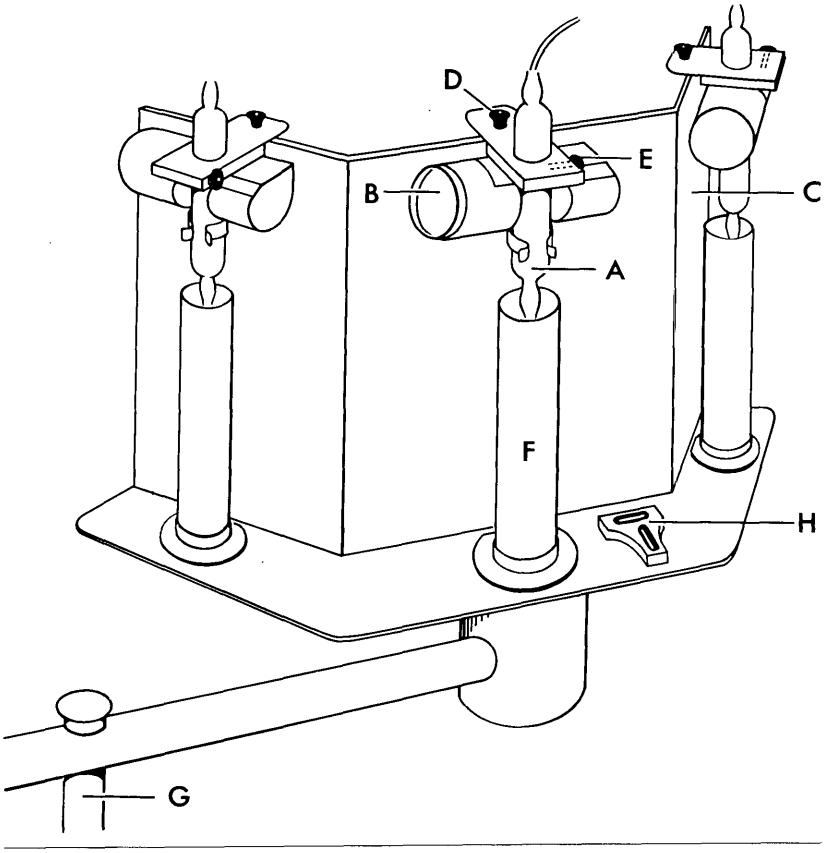
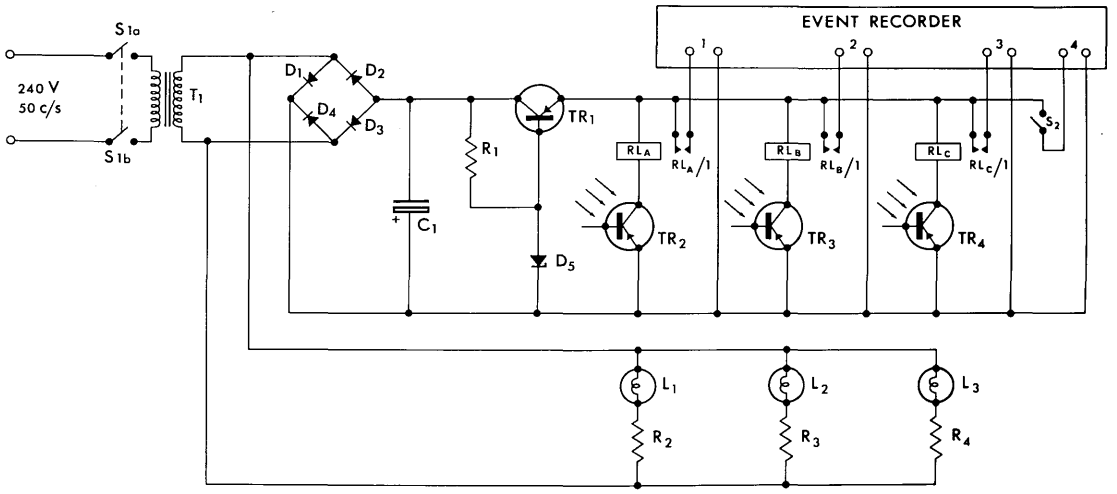


DIAGRAM OF APPARATUS FOR RECORDING PATTERN OF SALIVARY FLOW

(A) Glass Drip Chamber
(B) Perspex housing containing phototransistor
(C) Angled metal plate
(D) Perspex slide
(E) Screw clamp
(F) Collection bottle
(G) Stand
(H) Spirit level

FIGURE I , 7



R_1	680		1W		R_3	133	5W
R_2	133		5W		R_4	133	5W
C_1	75	MFD	50V				
TR_1	OC	35			TR_3	OCP	71
TR_2	OCP	71			TR_4	OCP	71
D_1	OA	210			D_4	CA	210
D_2	OA	210			D_5	SZ	24C
D_3	OA	210					

T_1	Mains transformer	Sec. 0-26 V I 8A
	L_1, L_2, L_3	Lamps 2 2 V 0 25A
	RL_A, RL_B, RL_C	Siemens High speed Relays Type H 96E 3400
	S_1 D.P.S.T.	Switch
	S_2 S.P.S.T.	Push button switch

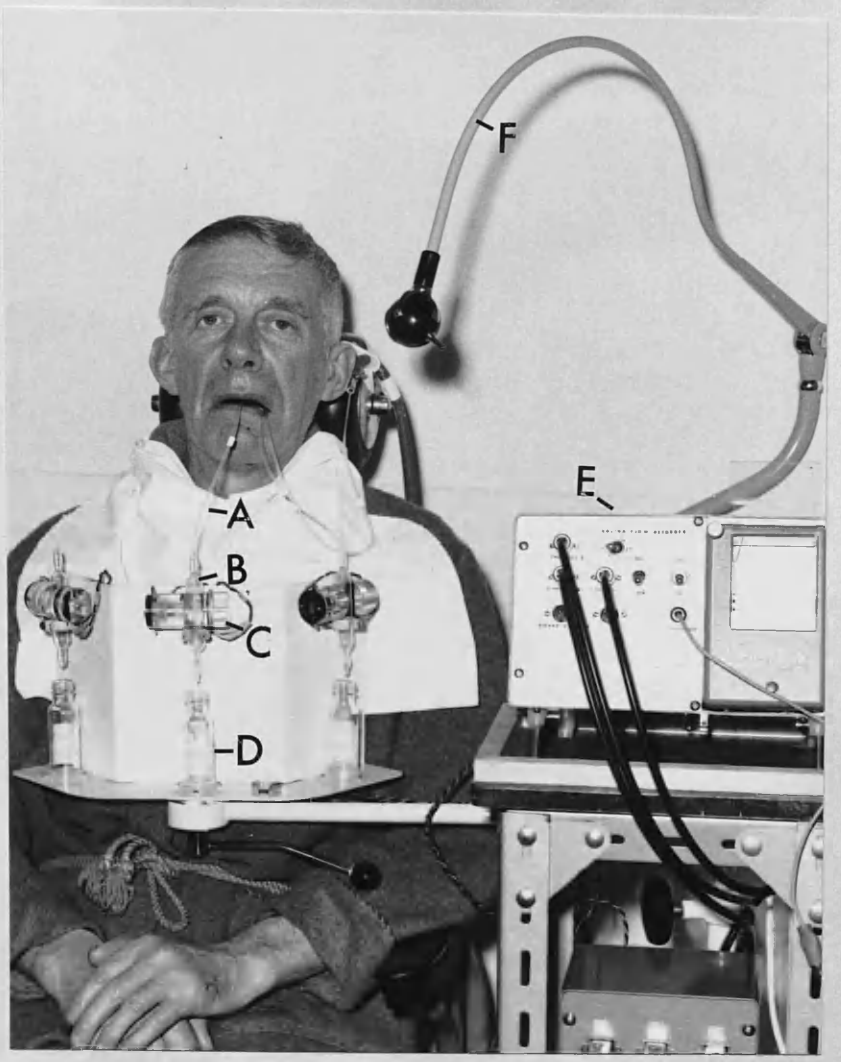
CIRCUIT DIAGRAM OF APPARATUS FOR RECORDING PATTERN OF SALIVARY FLOW

FIGURE I, 8

STIMULI USED TO PRODUCE DIFFERENT SALIVARY FLOW RATES

The Stimuli - paraffin wax, salt, 'boiling', fruit gums, oxo, and lemon juice.
The volumes of saliva collected in the same time period (5 minutes) in one subject are also shown.

FIGURE I, 9



THE 3-CHANNEL PHOTOELECTRIC SALIVARY FLOWMETER IN USE:

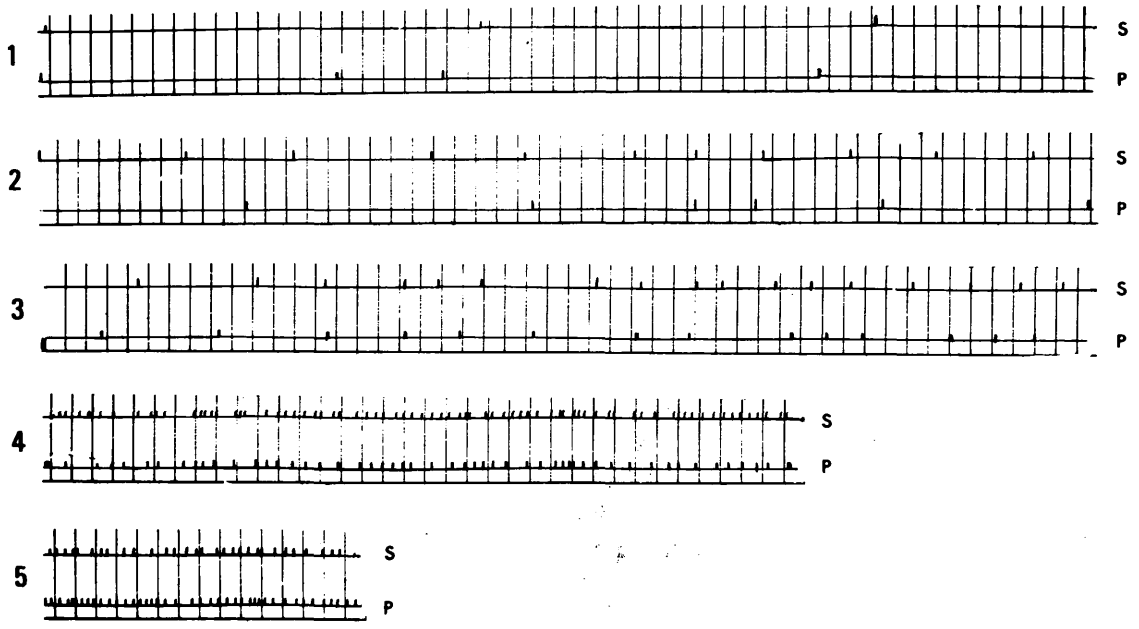
(A) Catheter - saliva
(B) Glass drip chamber
(C) Photo-electric detector
(D) Collecting bottle
(E) Event recorder
(F) Chairside lamp

FIGURE I, 10

A MODIFICATION TO THE ORIGINAL APPARATUS SHOWN IN FIG. I, 9.

Calibrated Tubes (A), (B) and (C) are used to collect saliva during an initial period of adjustment or between collection periods with different stimuli. When handle (H) is turned saliva is collected in tubes (X) (Y) and (Z) for analysis of constituents. Handle (H) simultaneously starts a timing device and the event recorder.

FIGURE I, 11



RECORDS OF PAROTID AND SUBMANDIBULAR SALIVARY FLOW PATTERN -

(1) 'resting'
(2) 'boiling' held in mouth,
(3) chewing paraffin wax,
(4) sucking 'boiling', and
(5) lemon juice.

S = Submandibular saliva P = Parotid saliva.

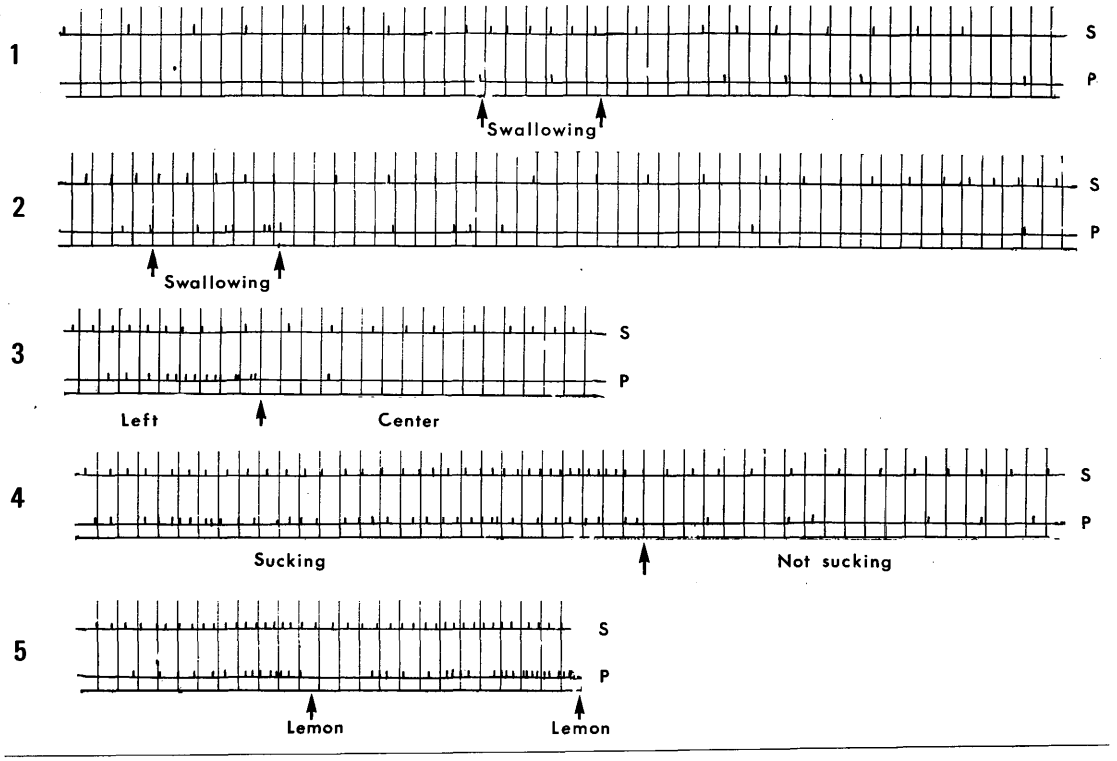
Vertical lines on paper correspond to 5 second intervals.

TABLE I, 1

Weight of saliva (g) per drop in 3 patients studied at different rates of flow. For each patient the drop size is relatively constant at each flow rate

Patient	'Resting'	Sucking 'boiling'	Lemon Juice
1	0.031	0.036	0.037
	0.032	0.034	0.038
	0.032	0.033	0.036
2	0.036	0.038	0.039
	0.033	0.038	0.040
	0.035	0.038	0.040
3	0.039	0.039	0.045
	0.036	0.040	0.043
	0.037	0.040	0.044

FIGURE I, 12



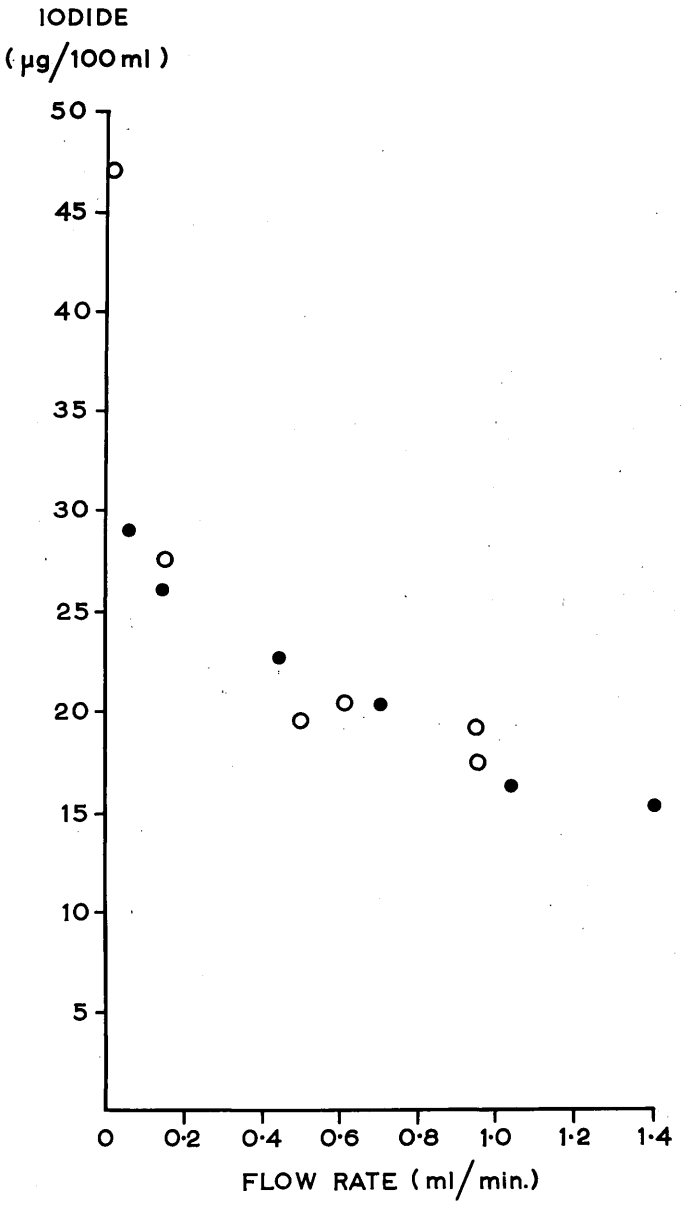
RECORDS OF PAROTID AND SUBMANDIBULAR SALIVARY FLOW PATTERNS SHOWING IRREGULARITIES.

Tracings read from right to left -

1) Increased rate with swallowing
2) Residual effect of lemon juice $1\frac{1}{2}$ minutes after stimulus discontinued
3) Effect of change in intra oral position of 'boiling' on flow rate
4) Effect of holding 'boiling' and sucking 'boiling'
5) Effect of intermittent stimulation with lemon juice.

S = Submandibular saliva P = Parotid saliva

FIGURE I, 13

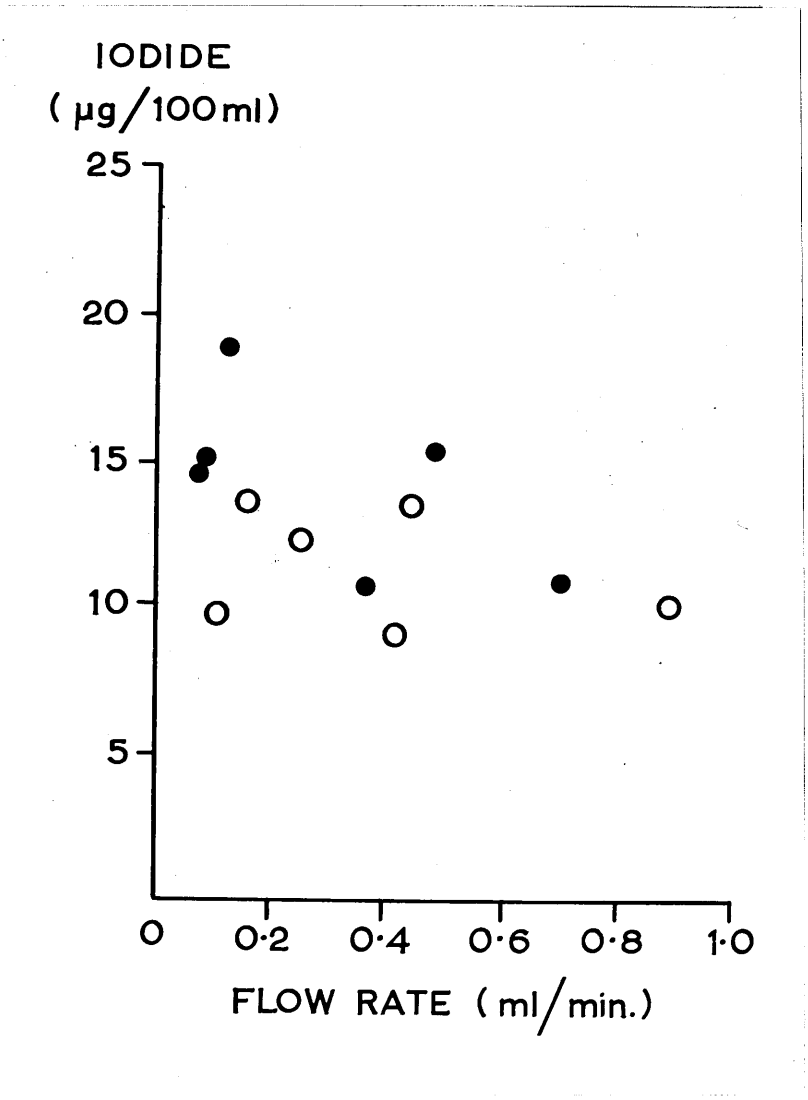


IODIDE CONCENTRATION IN PAROTID AND SUBMANDIBULAR SALIVA AT DIFFERENT FLOW RATES

● Submandibular saliva

0 Parotid saliva.

FIGURE I, 14

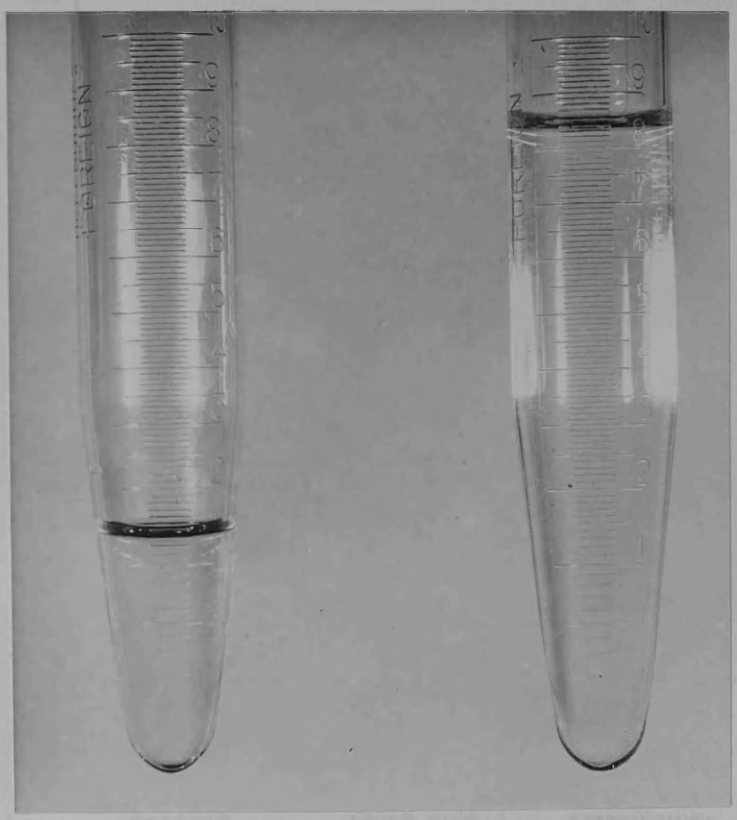


IODIDE CONCENTRATION IN PAROTID AND SUBMANDIBULAR SALIVA AT DIFFERENT FLOW RATES. THE FLOW RATE DURING EACH COLLECTION PERIOD WAS NOT REGULAR.

● Submandibular saliva

0 Parotid saliva

FIGURE I, 15

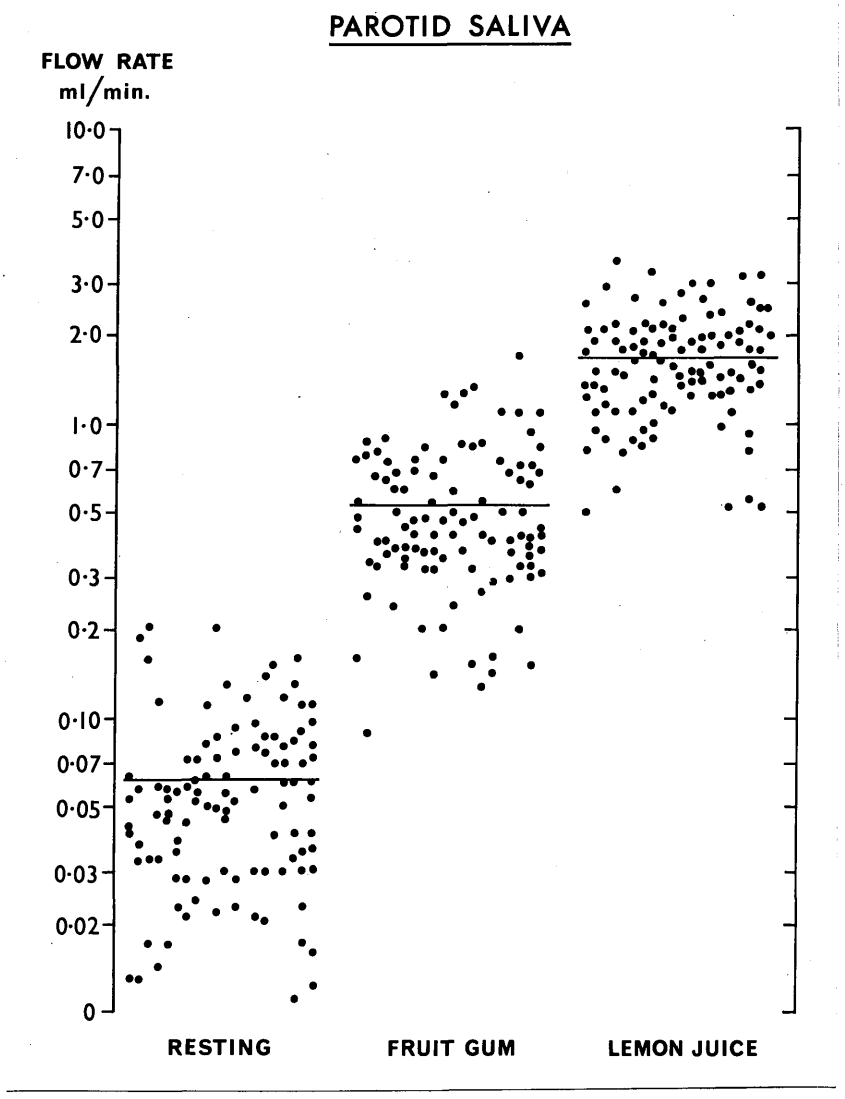


SALIVARY VOLUMES COLLECTED FROM (R) PAROTID GLAND DURING TWO FIVE MINUTE COLLECTION PERIODS CHEWING FRUIT GUMS AS THE STIMULUS.

(A) Chewing on (L) side only - volume = 1.5 c.c.

(B) Chewing on (R) side only - volume = 8.5 c.c.

FIGURE I, 16



PAROTID SALIVARY FLOW RATE (LOG SCALE) UNDER 'RESTING' CONDITIONS AND IN RESPONSE TO SUCKING FRUIT GUM AND LEMON JUICE STIMULATION IN 93 NORMAL SUBJECTS

'Resting'	saliva	collected	for	30	minutes
Fruit gum stimulation	"	"	"	5	"
Lemon juice	"	"	"	"	2	"

——— = Mean

TABLE I, 2

PAROTID FLOW RATES IN 93 NORMAL SUBJECTS (ml/min)

	AGE	'RESTING'	FRUIT GUM	LEMON JUICE
RANGE	12-75	0.01-0.20	0.09-1.70	0.50-3.60
MEAN	47.50	0.06	0.53	1.66
S.E.M.	1.690	0.004	0.030	0.060

'Resting' Saliva collected for 30 min.

Stimulated Fruit Gum Saliva collected for 5 min.

Stimulated Lemon Juice Saliva collected for 2 min.

TABLE I, 3

SALIVARY FLOW RATES (VOL/MIN) FROM RIGHT AND LEFT PAROTID GLANDS IN 12 SUBJECTS.

Simultaneous bilateral collections were taken during a period of 2 minutes with lemon juice stimulation.

(ml/min)

SUBJECT	RIGHT SIDE	LEFT SIDE
1	1.40	1.52
2	2.35	2.39
3	1.90	2.10
4	3.63	3.25
5	2.60	2.71
6	1.53	1.51
7	1.24	1.32
8	1.45	1.40
9	1.02	0.93
10	2.10	1.95
11	2.42	2.49
12	0.89	0.86

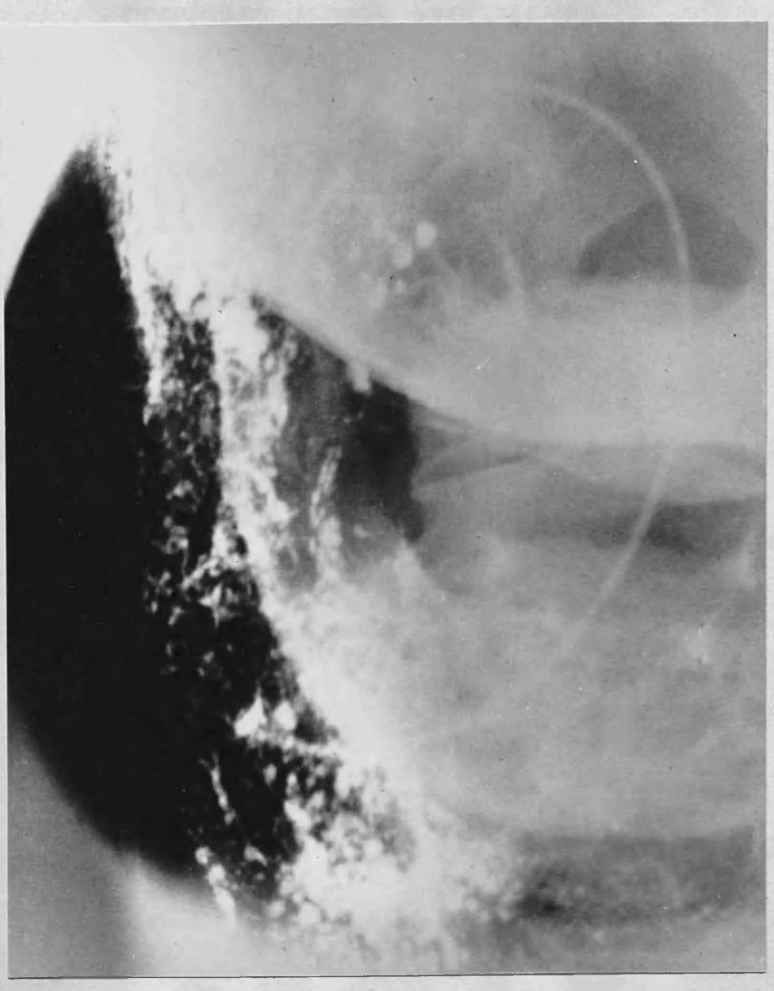
TABLE 1, 4

RESULTS OF STANDARD TEST ON 10 SUBJECTS CARRIED OUT ON THREE CONSECUTIVE DAYS AT THE SAME TIME EACH DAY AND SAME TIME INTERVAL AFTER MEALS.

(ml/min)

	RESTING			FRUIT GUM			LEMON JUICE		
DAY	1	2	3	1	2	3	1	2	3
SUBJECT 1.	0.04	0.08	0.16	0.38	0.62	0.30	1.90	2.50	2.00
2.	0.02	0.07	0.04	0.83	1.07	0.94	1.30	1.35	1.25
3.	0.03	0.07	0.11	0.37	0.15	0.36	1.40	1.40	1.50
4.	0.12	0.05	0.11	0.64	0.68	0.72	1.35	1.90	1.85
5.	0.03	0.13	0.03	0.41	0.42	0.50	3.30	2.60	2.30
6.	0.04	0.08	0.07	0.60	0.42	0.37	1.25	1.26	1.21
7.	0.08	0.09	0.11	0.58	0.90	1.08	2.40	2.90	2.25
8.	0.06	0.05	0.04	0.75	0.62	0.81	1.56	1.64	1.81
9.	0.04	0.06	0.05	1.10	0.59	0.85	1.45	1.47	1.49
10.	0.02	0.03	0.02	0.40	0.29	0.35	2.20	2.07	2.22
MEAN	0.05	0.07	0.07	0.61	0.58	0.63	1.81	1.91	1.79
S.E.M.	0.010	0.009	0.015	0.075	0.087	0.090	0.208	0.185	0.129

FIGURE I, 17



RETENTION OF CONTRAST MEDIUM IN TISSUES AROUND PAROTID AND SUBMANDIBULAR GLANDS.

Patient with Sjögren's syndrome reported having had sialographic examination six months previously by hand injection technique.

TABLE I, 5

PHYSICAL PROPERTIES OF SIALOGRAPHIC CONTRAST MEDIA AND SALIVA

Comparison of Specific Gravity and Viscosity of 3 types of Contrast Media and Parotid and Submandibular saliva

		S.G.	VISCOSITY at 37°C (centipoises)
CONTRAST MEDIA -	Water Soluble (TRIOSIL '45')	1.280	2.9
	Iodised ethyl esters (NEOHYDRIOL FLUID)	1.280	9.6
	Iodised Oil (NEOHYDRIOL VISCOUS)	1.375	12.0
'RESTING' SALIVA	PAROTID	1.000-1.003*	1.5+
	SUBMANDIBULAR	1.001-1.004*	3.4+

+ The figures for Salivary Viscosity are those of Schneyer (1955)

* The figures for Salivary Specific Gravity are those of Kerr (1961)

FIGURE, I, 18

MEASUREMENT OF SALIVARY GLAND SECRETING PRESSURE.

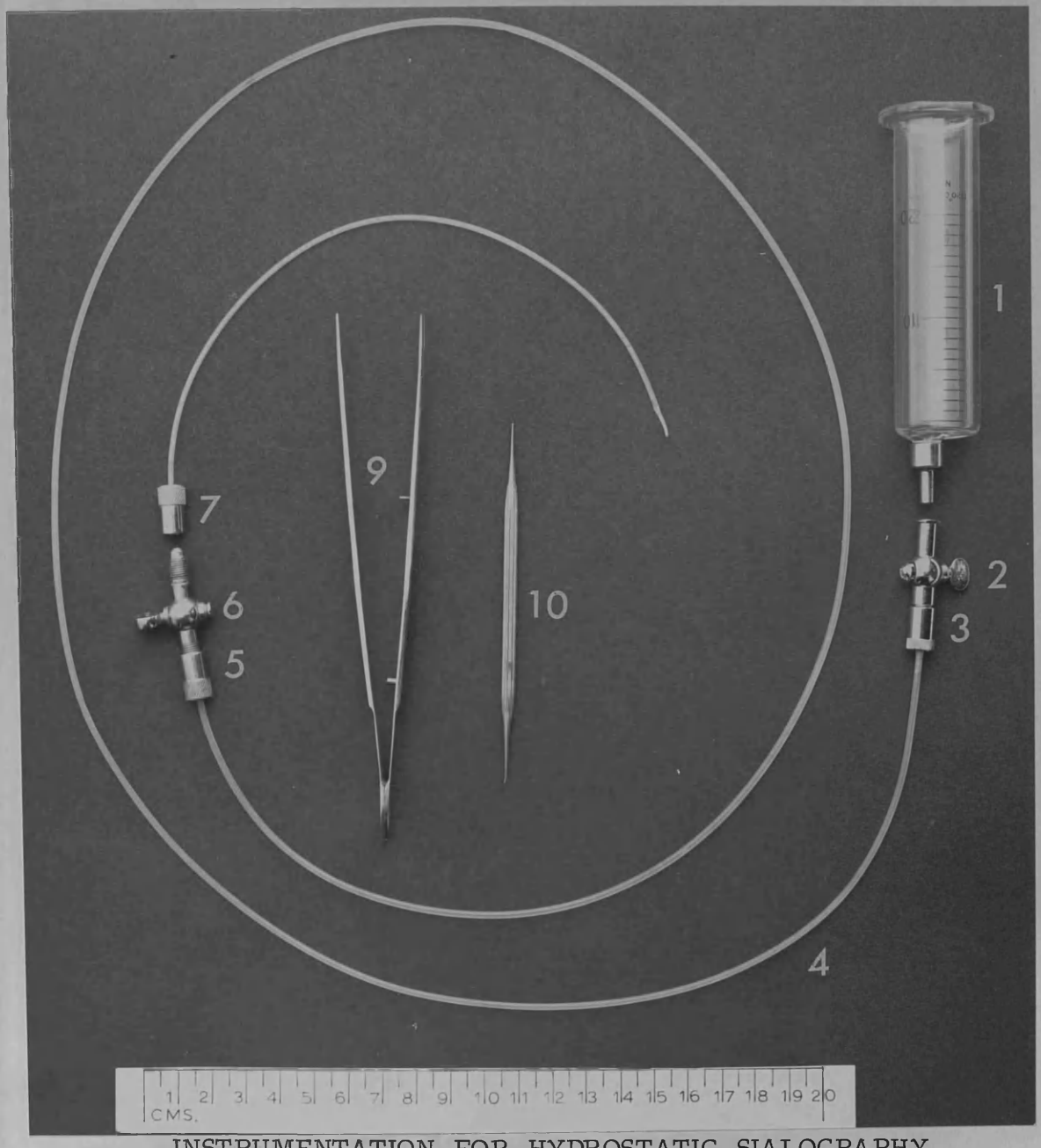
Apparatus consists of a metrestick to which catheter from the duct is attached. The height of the saliva meniscus within the catheter above the mid-point of the gland under investigation is measured in cms.

TABLE I, 6

SECRETING PRESSURES (cms of H_2O) OF PAROTID AND SUBMANDIBULAR GLANDS UNDER 'RESTING' AND STIMULATED CONDITIONS (sucking fruit gum)

PAROTID		SUBMANDIBULAR	
'Resting'	Stimulated	'Resting'	Stimulated
12	62	14	74
22	54	14	70
26	70	22	62
10	68	25	58
40	72	18	58
22	65	12	73
8	60	13	72
16	54	17	70
0	70	22	74
23	62	18	70
5	65	14	73
15	68	15	69
20	58	21	72
16	54	12	74
7	64	23	69
24	67	19	68
29	71	12	74
0	59	18	73
RANGE 0-40	54 - 72	12 - 25	58 - 74
MEAN 16.4	63.5	17.1	69.6
S.E.M. 2.48	1.41	0.97	1.26

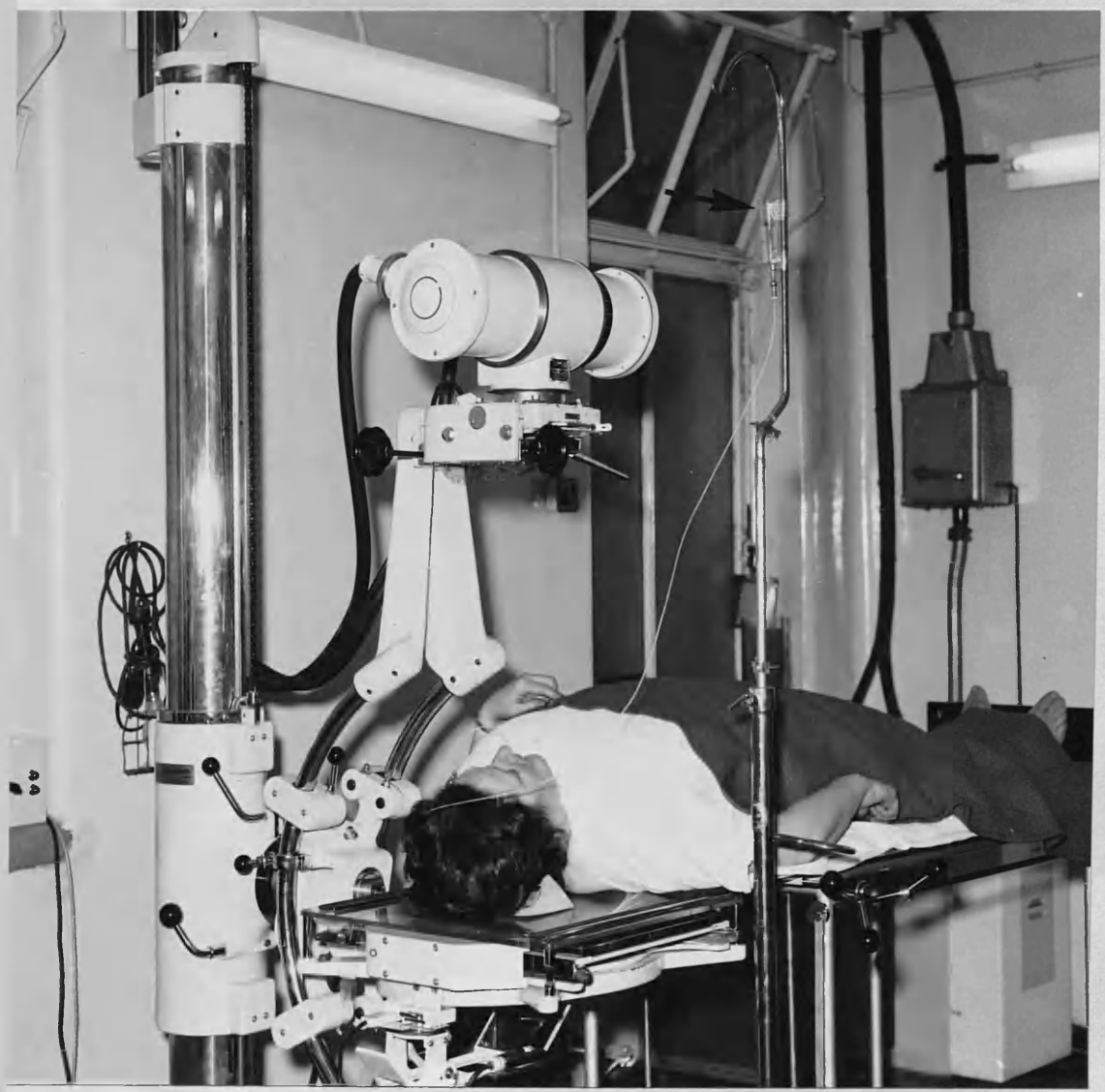
FIGURE I , 19



INSTRUMENTATION FOR HYDROSTATIC SIALOGRAPHY

1. 20 cc. Glass syringe barrel
2. Adaptor 3. Cap
4. Portex polythene tubing P.E. 205
5. Cap 6. Adaptor 7. Cap
8. Portex polythene tubing P.E. 160 tapered at one end
9. Tissue forceps non-toothed
10. Lacrimal probe dilator

FIGURE 1 , 20

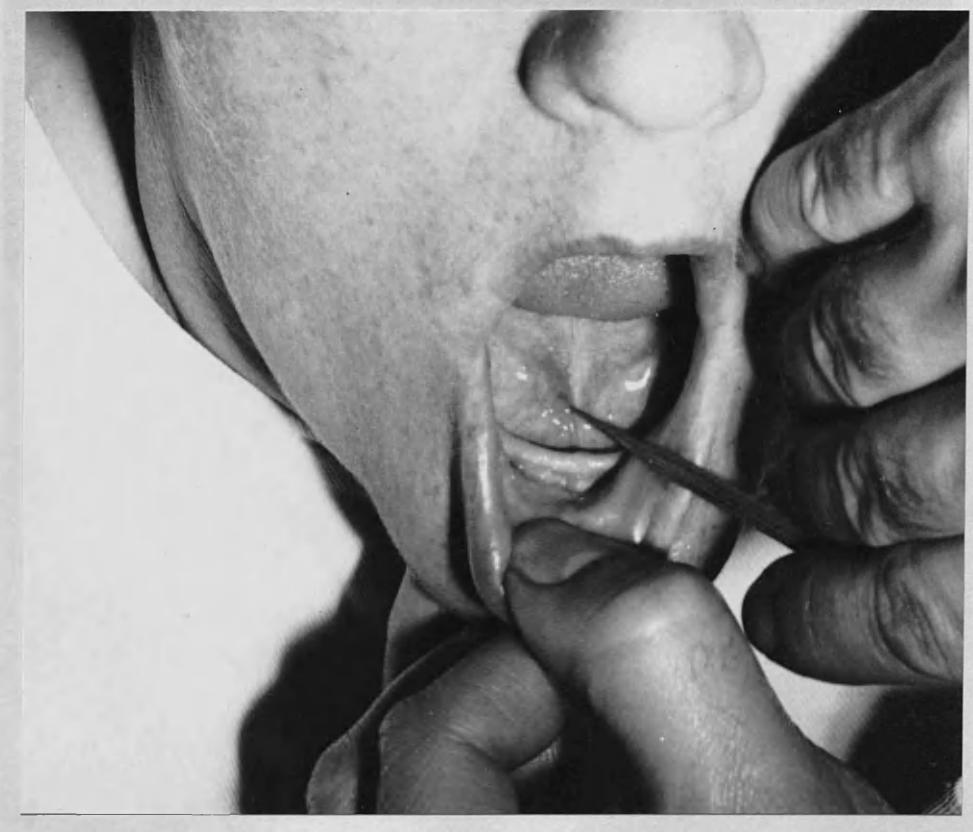


APPARATUS ASSEMBLED PRIOR TO SIALOGRAPHY

(A) Passive Filling Phase: With the apparatus assembled and the patient lying horizontally on an ELEMA-SCHONANDER SKULL TABLE the syringe barrel (arrowed) is filled with contrast 'TRIOSIL 45' (Sodium Metrizoate). The contrast is allowed to run freely through the catheter system to expel all air bubbles. The tapered end of the catheter is then introduced .5-1 cm. into the salivary duct.

(b) Active emptying phase: The patient is given a slice of lemon to suck immediately after the passive filling phase exposures have been completed and the catheter removed from the duct. After a 5-minute period a further two exposures are made - antero-posterior and lateral oblique of the parotid gland region and a lateral view of the submandibular gland. If the gland is functioning normally no contrast medium should be demonstrated.

FIGURE I, 21



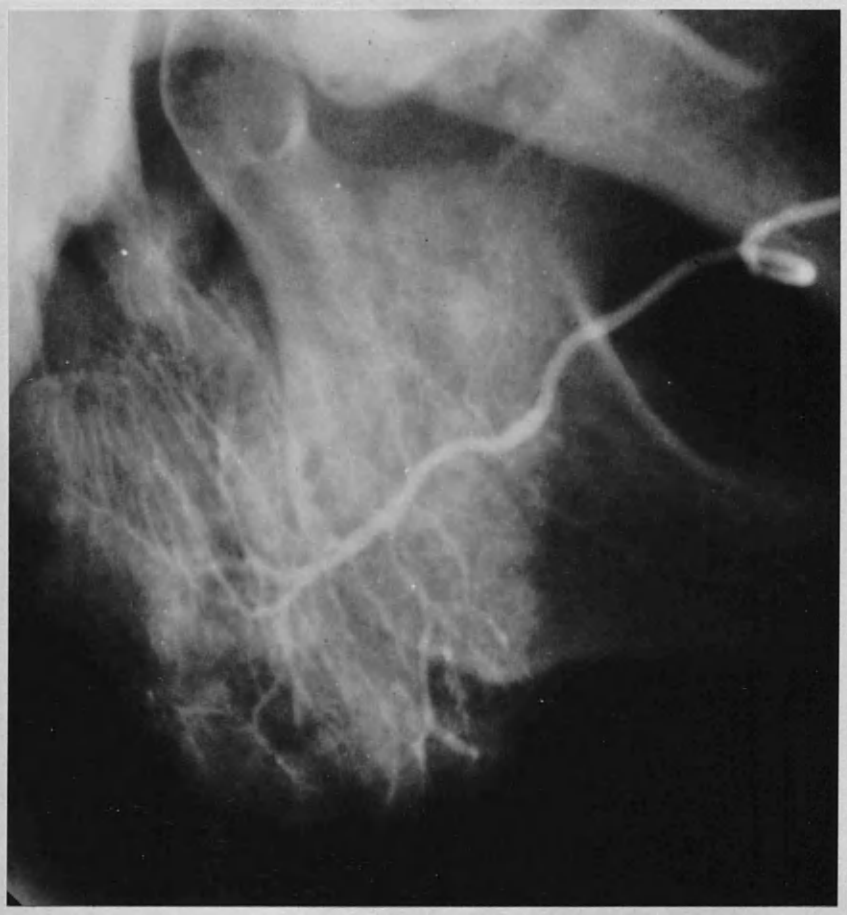
IDENTIFICATION AND DILATATION OF SUBMANDIBULAR DUCT ORIFICE USING A LACRIMAL PROBE DILATOR.

FIGURE I , 22

POLYETHYLENE CATHETER IN POSITION -

SUBMANDIBULAR DUCT.

FIGURE I , 23



NORMAL SIALOGRAM (FILLING PHASE)

PAROTID - Lateral oblique view.

FIGURE I , 24

NORMAL SIALOGRAM (FILLING PHASE)

PAROTID - Antero-posterior view.

FIGURE I , 25

NORMAL SIALOGRAM (FILLING PHASE)

SUBMANDIBULAR - Lateral oblique view.

FIGURE I, 26

SJÖGREN'S SYNDROME - FILLING PHASE
LATERAL OBLIQUE VIEW OF (L) PAROTID GLAND

There is poor peripheral duct filling and punctate collections of contrast of "Mulberry bush" type typical of moderate changes in this disease.

FIGURE I , 27

SJÖGREN'S SYNDROME - SECRETORY PHASE
LATERAL VIEW OF (L) PAROTID GLAND

There is retention of contrast medium in the punctate areas after the main ducts have emptied.

FIGURE I, 28

LARGE SUBMANDIBULAR DUCT CALCULUS

Sialographic appearances of large calculus in dilated submandibular duct. The water soluble contrast medium has flowed past the calculus and into the submandibular gland.

FIGURE I, 29

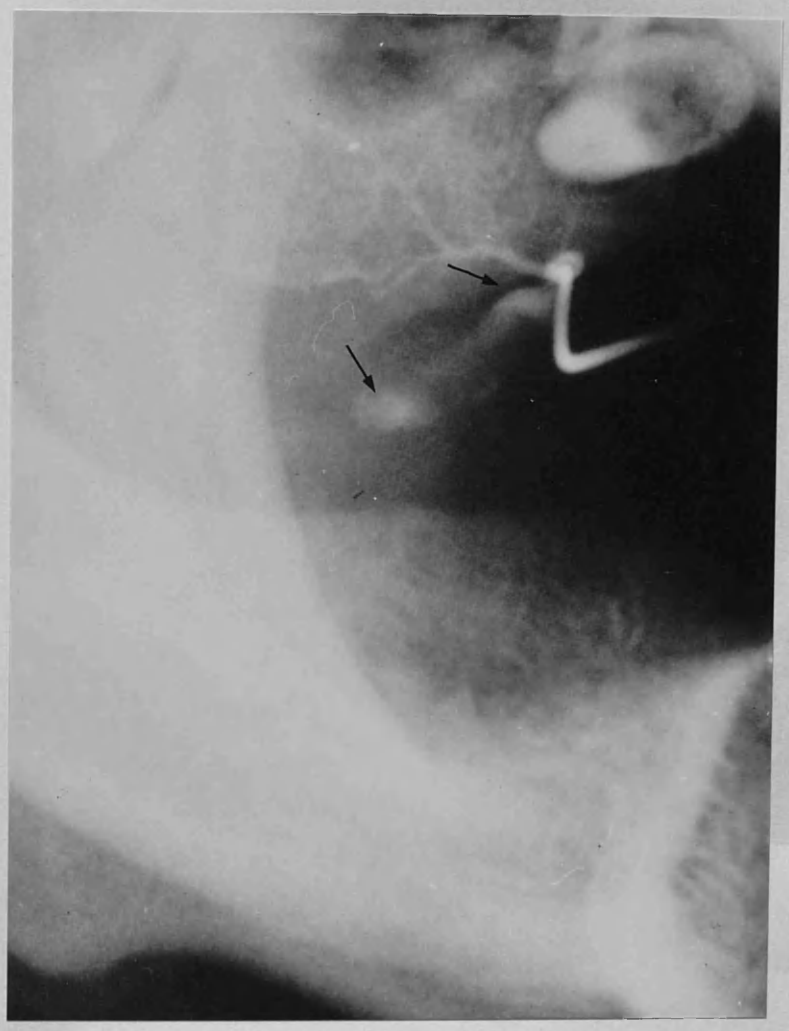
CHRONIC PAROTITIS

ANTERO-POSTERIOR VIEW OF (R) PAROTID GLAND

(A) Passive filling phase showing gross sialectasis with cavitation

(B) Secretory phase - contrast remains.

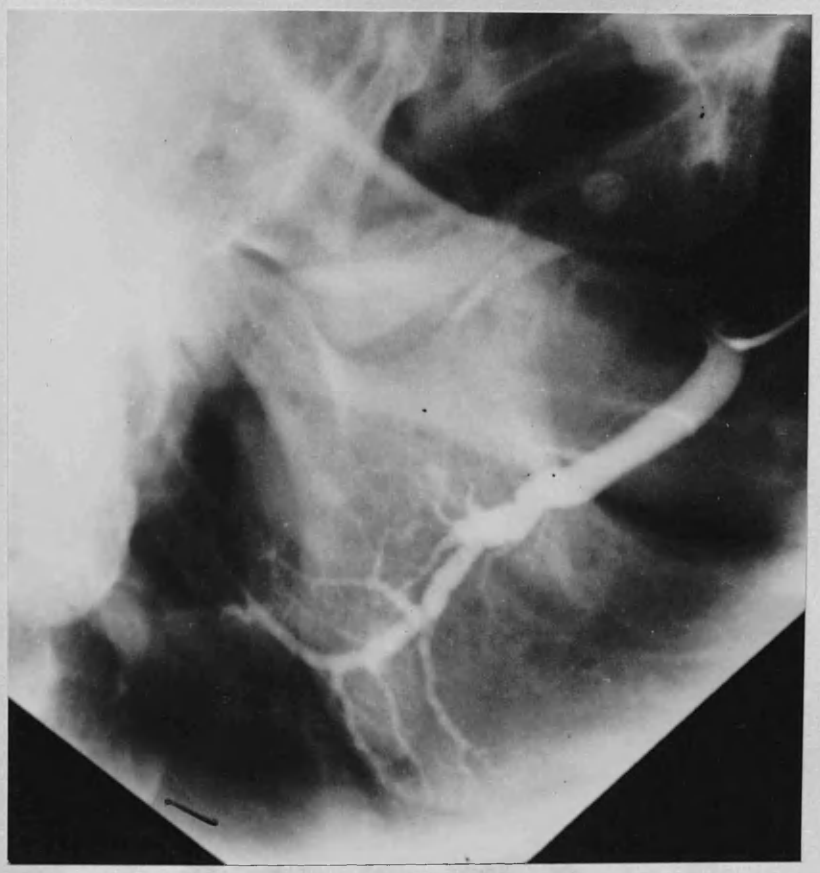
FIGURE I, 3O



PAROTID DUCT CALCULUS - LATERAL OBLIQUE VIEW

A large translucent calculus (arrowed) faintly outlined by contrast near the orifice of the main parotid duct. An impacted upper canine tooth is present above.

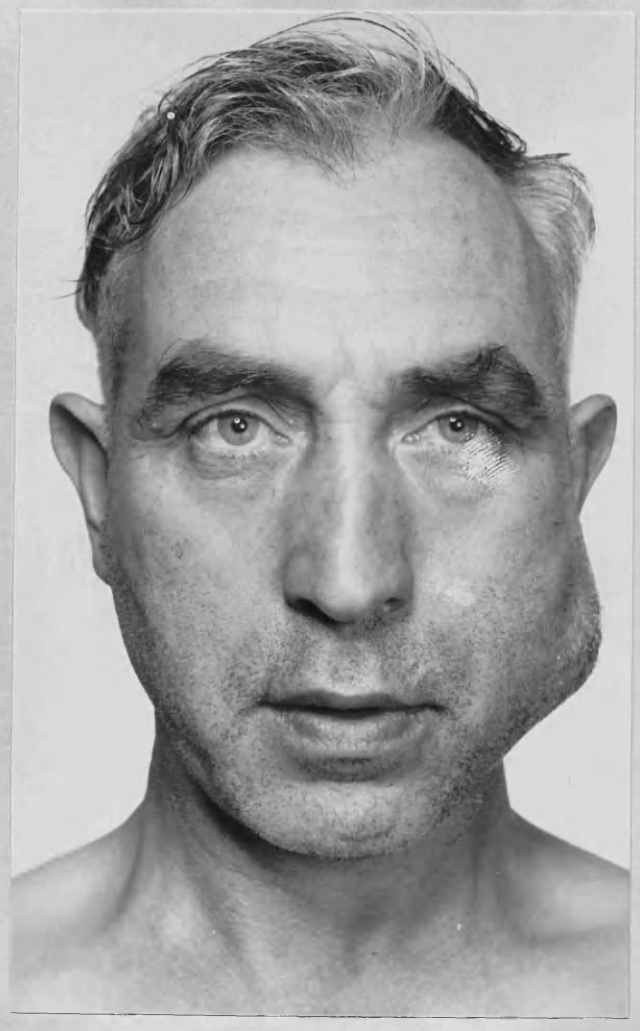
FIGURE I, 31



CHRONIC OBSTRUCTION (L) PAROTID GLAND
LATERAL OBLIQUE VIEW

A grossly dilated main parotid duct, with peripheral duct distention and poor terminal duct filling due to chronic obstructive disease. This sialogram was performed after the passage of a parotid duct calculus.

FIGURE I, 32



PAROTID GLAND FISTULA

Patient with swelling of left parotid region after a lacerating wound of face two weeks before. Characteristic history of increasing swelling at meals. (Sialogram Fig. I, 33)

FIGURE I, 33

PAROTID FISTULA - SIALOGRAM
(of patient Fig. I, 32)

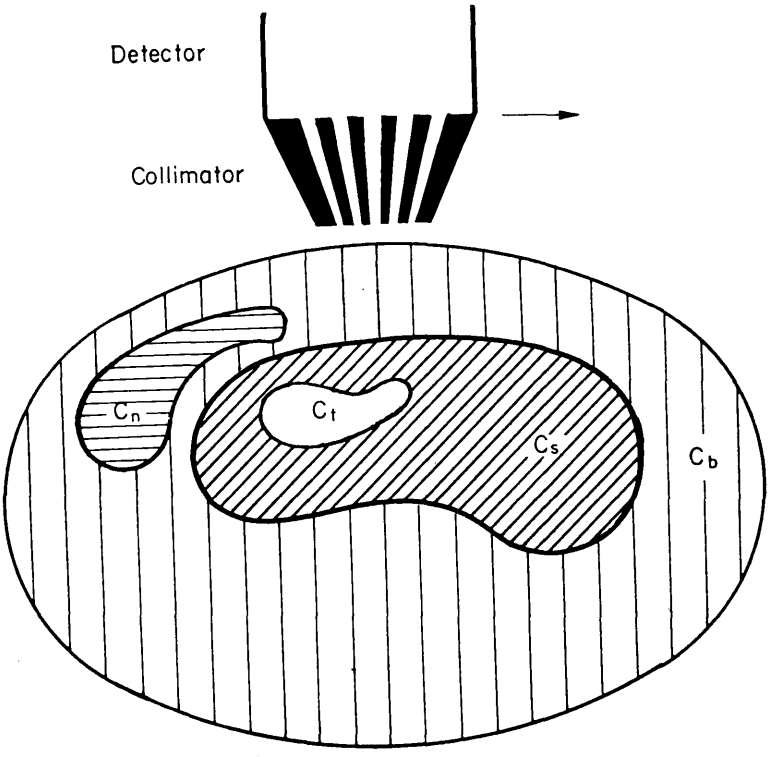
Antero-posterior view of (L) parotid gland showing division (arrowed) of a branch of (L) parotid duct. There is accumulation of contrast outwith the gland.

TABLE I, 7

PHYSICAL CHARACTERISTICS AND RADIATION DOSE OF ISOTOPES USED

Isotope	Tracer Dose	Physical half life	Effective half life in Salivary Gland	Energies (M.e.v.)	Energies (M.e.v.)	Av. Energies (M.e.v.)	Gamma Dose Rate Constant (cm^2-r/mc.hr.)	Absorbed dose (rads) (from radiation)	Absorbed dose (rads) (from radiation)	Total Absorbed dose due to tracer dose (rads)
^{131}I	25 μc	8.05 days	0.3 days	.61, .34, .25	.72 (3%) .64 (9%). 36(81%) .28 (6%). 08(6%)	0.19	2.18	0.32	0.085	0.40
^{132}I	50 μc	0.097 days	0.073 days	2.1, 1.6, 1.2, .97, 73	2.2 (2%) 1.9(5%) 1.41(13%) 1.14(9%) 0.97(23%) 0.76(93%) 0.67(100%) 0.62(6%) 0.52(30%)	0.48	11.8	0.40	0.22	0.62
^{82}Br	30 μc	1.49 days	0.27 days	0.44	1.47(18%)1.32(27%) 1.04 (3%)0.83(25%) 0.77(82%)0.69(30%) 0.62(48%)0.55(75%)	0.135	14.6	0.016	0.041	0.057
$^{99m}TcO_4^-$	500 μc	0.25 days	0.14 days		0.14		0.56		0.094	0.094

FIGURE I , 34



THE SIMPLIFIED CLINICAL SCANNING PROBLEM (AFTER MALLARD, 1966).

The target (concentration C_t) is embedded in surrounding tissue (C_s) with a neighbouring structure (C_n) contained within the general body background (C_b) which includes scattered radiation.

FIGURE I , 35

PICKER MAGNASCANNER V

The patient lies horizontally on the table and the scanner head (A) moves over the area of the salivary glands. The radioactivity is recorded on a chart placed on the table (B).

FIGURE I, 36

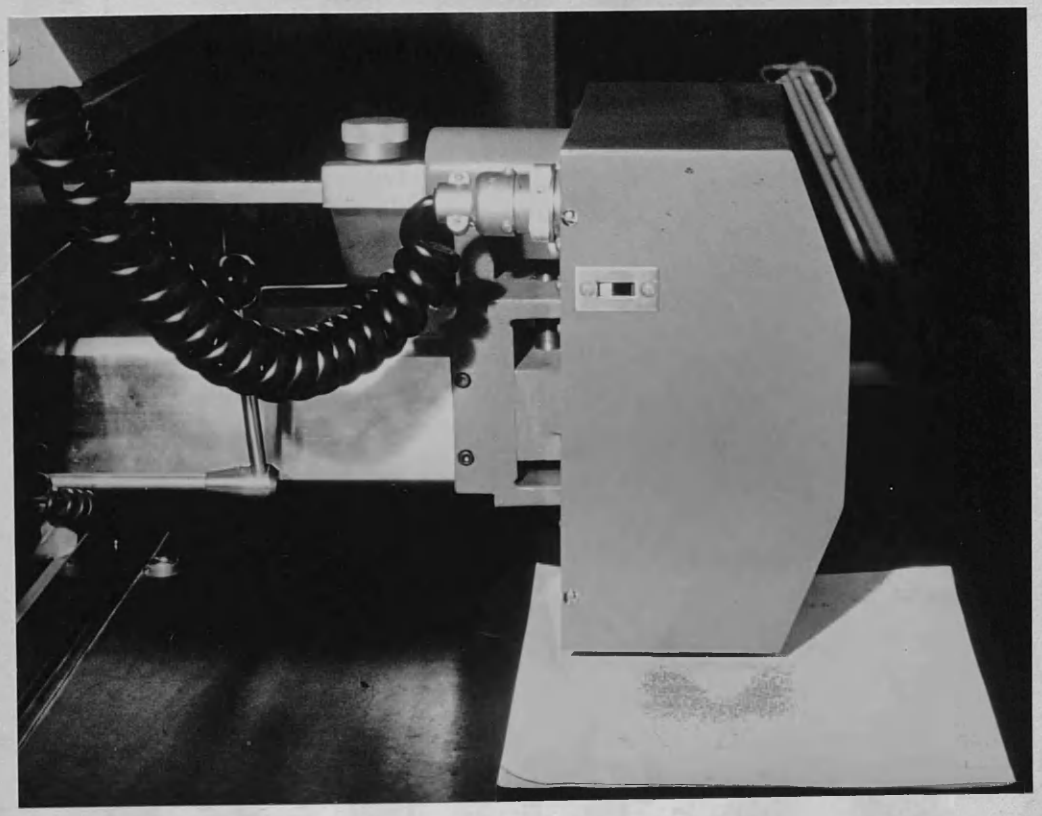


CHART TABLE WITH HEAD AND NECK SCAN IN PROGRESS

TABLE I, 8

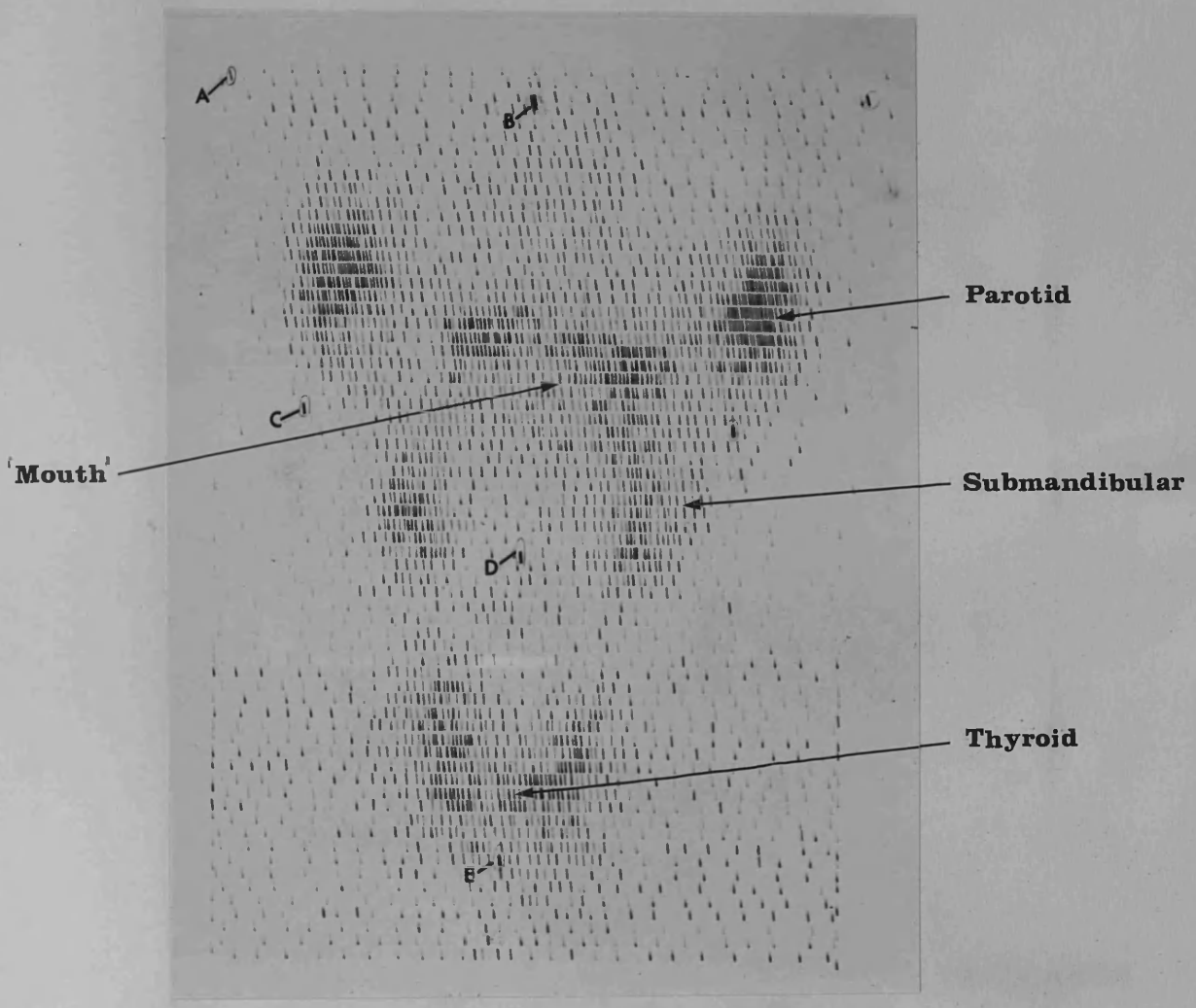
UPTAKE OF $^{99m}TcO_4$ BY THE THYROID AND SALIVARY GLANDS
30-35 MINS. AFTER INJECTION OF A TRACER DOSE (% DOSE)

PATIENT	THYROID	SUBMANDIBULAR (R)	SUBMANDIBULAR (L)	PAROTID (R)	PAROTID (L)	MOUTH
1	0.95	0.61	0.60	+	+	0.66
2	1.51	0.29	0.26	0.32	0.33	0.20
3	1.19	0.46	0.44	0.74	0.80	0.99
4	0.34	0.08	0.07	0.12	0.10	0.06
5	1.37	0.17	0.04	0.12	0.08	0.06
6	0.35	⁂	⁂	0.31	0.34	0.77 ⁂
7	1.00	0.75	0.40	0.48	0.48	0.06
MEAN	0.96	0.39	0.30	0.35	0.36	0.32
S.E.M.	0.174	0.106	0.090	0.096	0.109	0.167

\+ Parotid gland areas not scanned in this patient

⁂ 0.77% represents the dose present in both submandibular glands and in the mouth, as these could not be clearly distinguished in the scan.

FIGURE I , 37

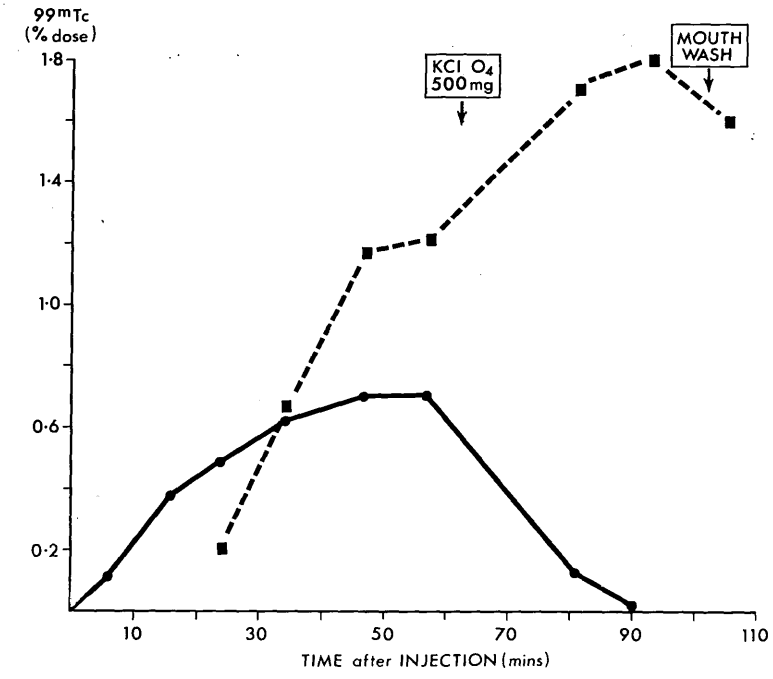


NORMAL SCAN 23-43 MINS. AFTER $^{99m}TcO_4$ 800 μc INTRAVENOUSLY

A = Upper margin of external ear
B = Bridge of nose
C = Angle of mandible
D = Mid-point of chin
E = Sternal notch

Thyroid, submandibular and parotid glands are outlined. Some radioactivity is seen centrally in the 'mouth' region.

FIGURE I, 38



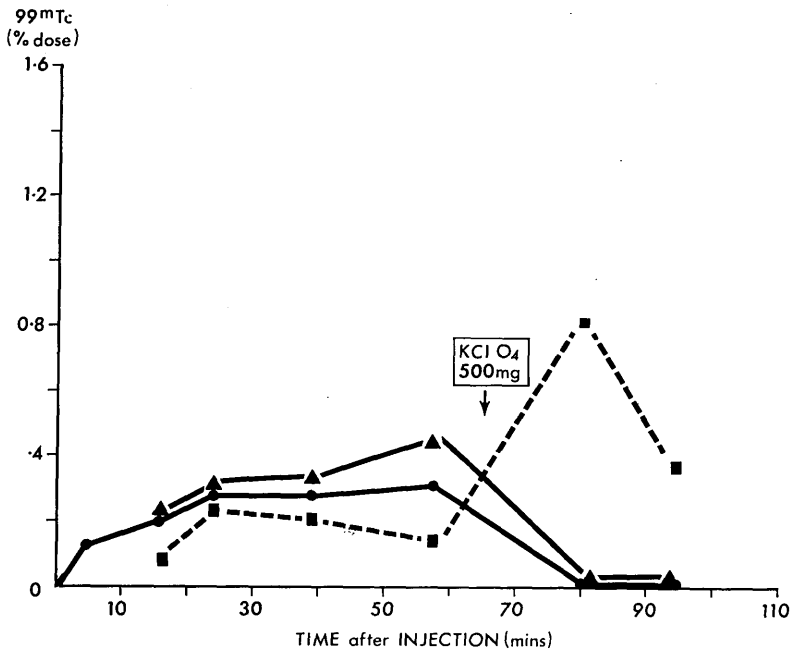
UPTAKE OF $^{99m}TcO_4$ BY SUBMANDIBULAR GLANDS FOLLOWING A TRACER DOSE INTRAVENOUSLY

●——● Submandibular gland uptake (mean of right and left)

■---■ Activity in the 'mouth' region.

Thyroid and salivary gland uptake is discharged by perchlorate. Activity in 'mouth' region increases with time and is not discharged by perchlorate or mouthwashing.

FIGURE I, 39

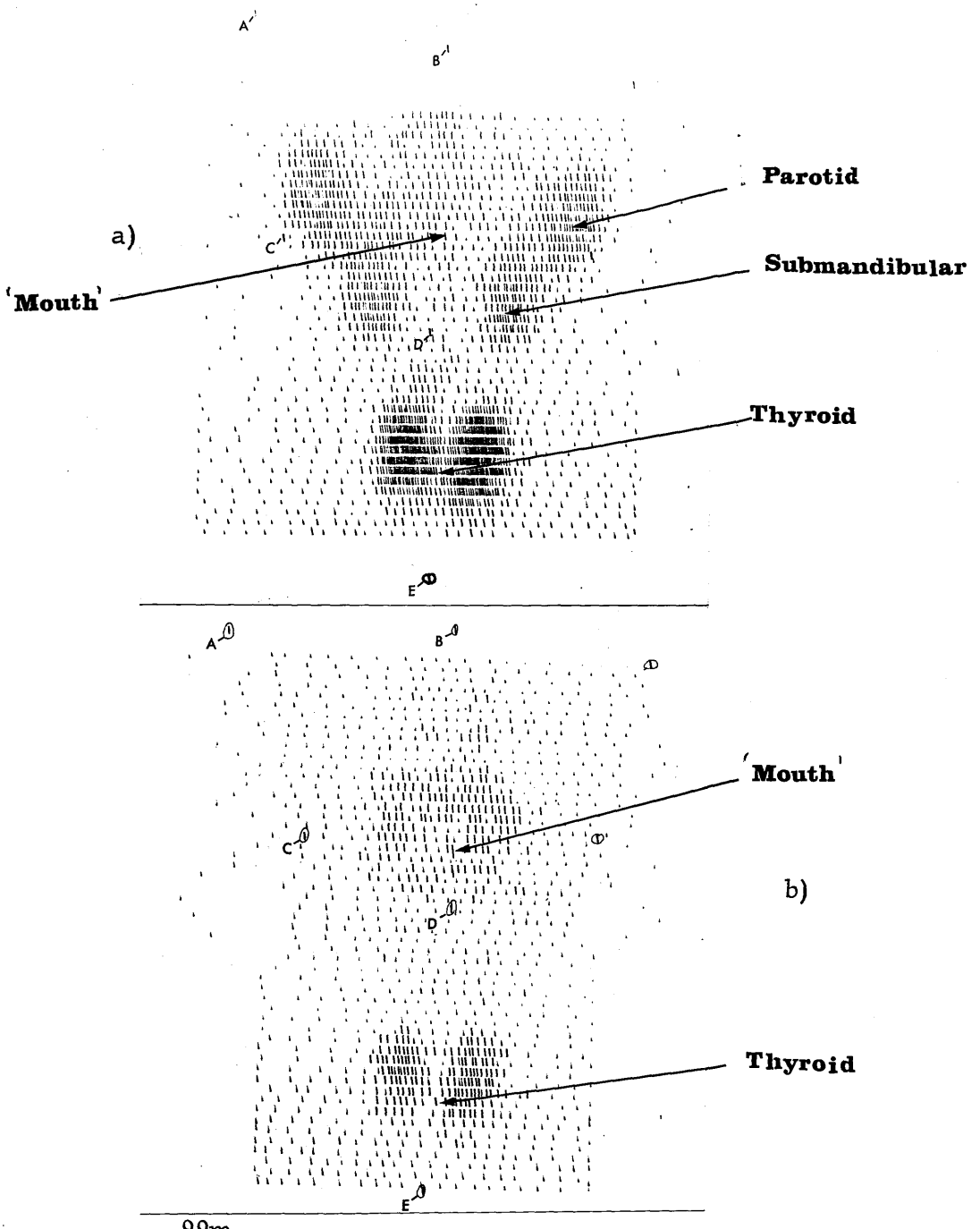


UPTAKE OF $^{99m}TcO_4$ BY SUBMANDIBULAR AND PAROTID GLANDS FOLLOWING A TRACER DOSE INTRAVENOUSLY.

●——● Submandibular gland uptake (mean of right and left)

▲——▲ Parotid gland uptake (mean of right and left)

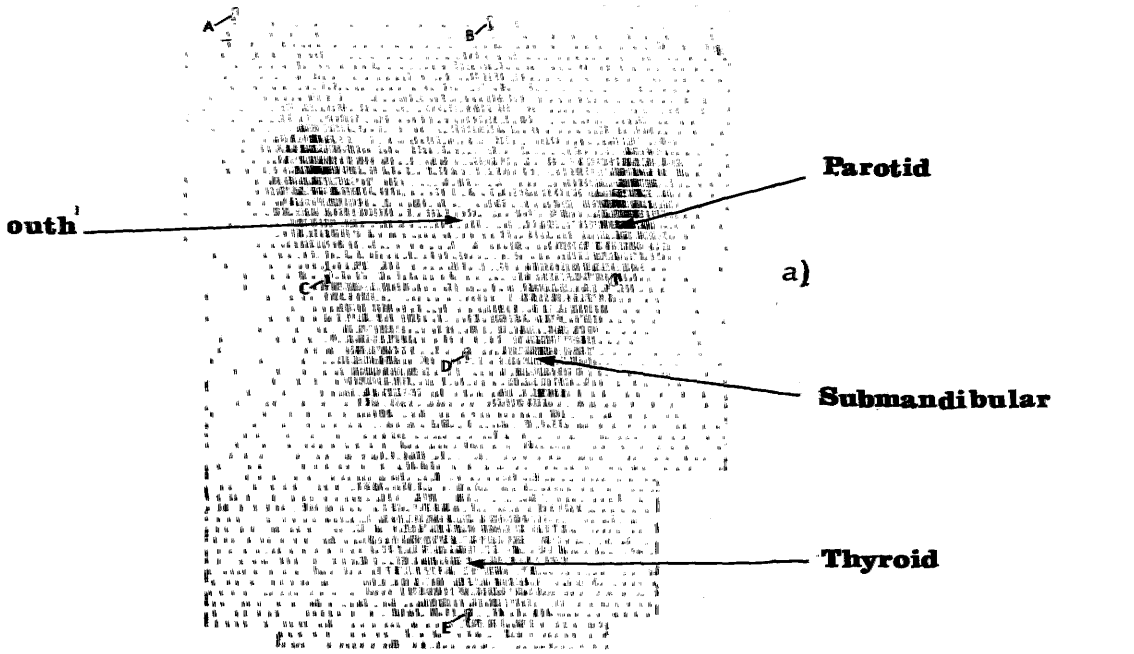
■-----■ Activity in 'mouth' region

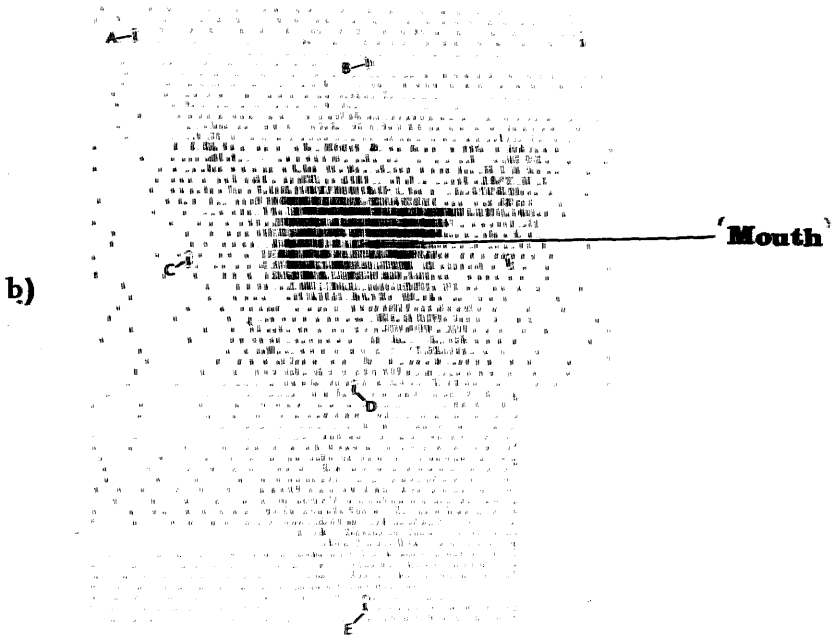


UPTAKE OF $^{99m}TcO_4$ BY SUBMANDIBULAR, PAROTID AND THYROID GLANDS AFTER A TRACER DOSE INTRAVENOUSLY

A = Upper margin of external ear B = Bridge of nose
C = Angle of mandible D = Mid-point of chin
E = Sternal notch

a) 18-38 minutes following tracer dose
b) 30-50 minutes after perchlorate administration.



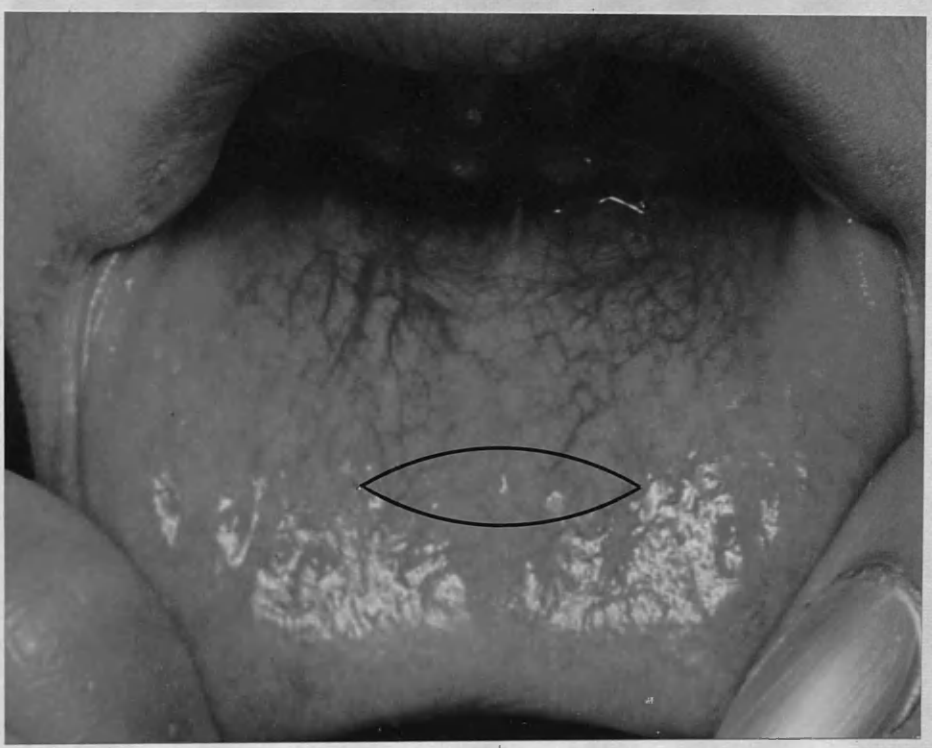


UPTAKE OF $^{99m}TcO_4$ OVER THYROID AND SALIVARY GLANDS AFTER ATROPINE 0.6 mgm SUBCUTANEOUSLY.

a) 23-43 min. after tracer dose. Radioactivity is seen in submandibular, and parotid glands and in the thyroid. Negligible amounts are seen in the 'mouth' region.

b) 147-167 mins. after tracer dose. Most radioactivity is seen in the 'mouth' region.

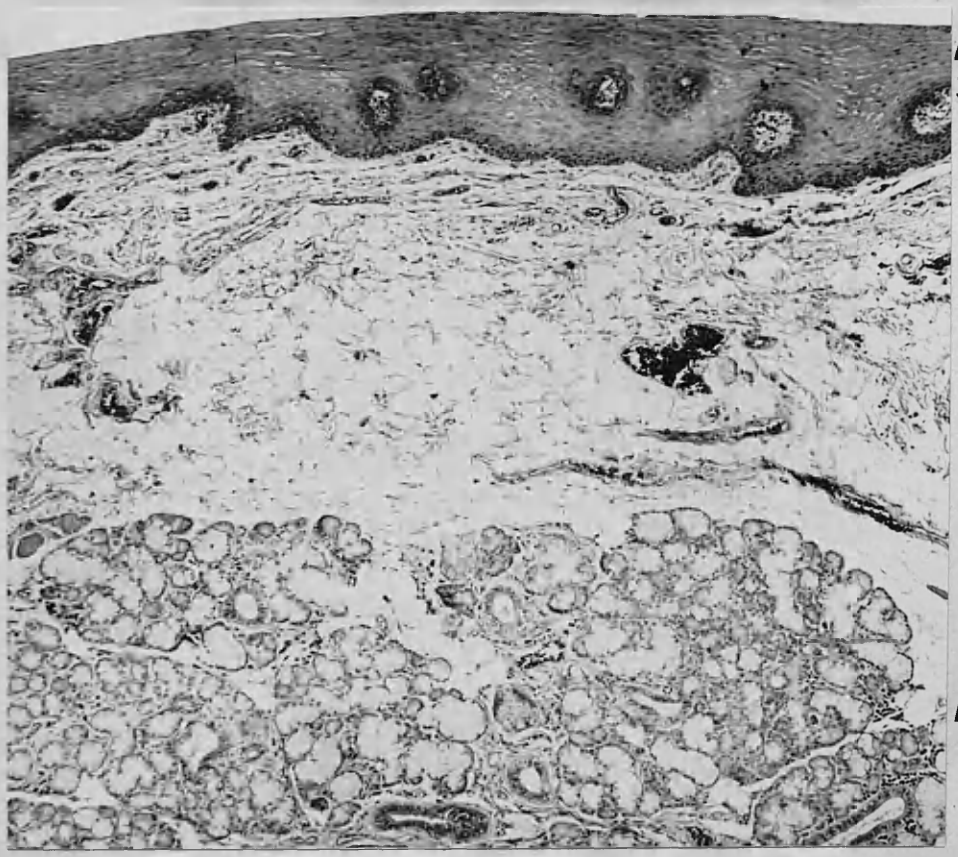
FIGURE I, 42



LABIAL GLAND BIOPSY

Area outlined inside lower lip 3 cms x .75 cms approx. to show site of labial biopsy.

FIGURE I, 43



LABIAL MUCOUS GLANDS

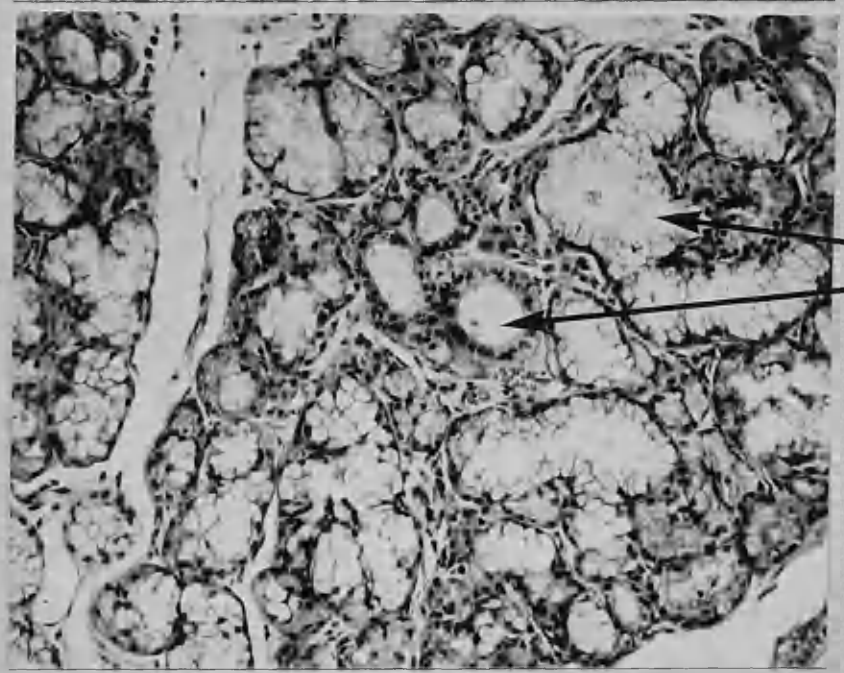
Photomicrograph showing proximity of labial mucous glands to mucosal surface. Stained H. & E.

Magnification x 75

FIGURE 1, 11

A)

B)

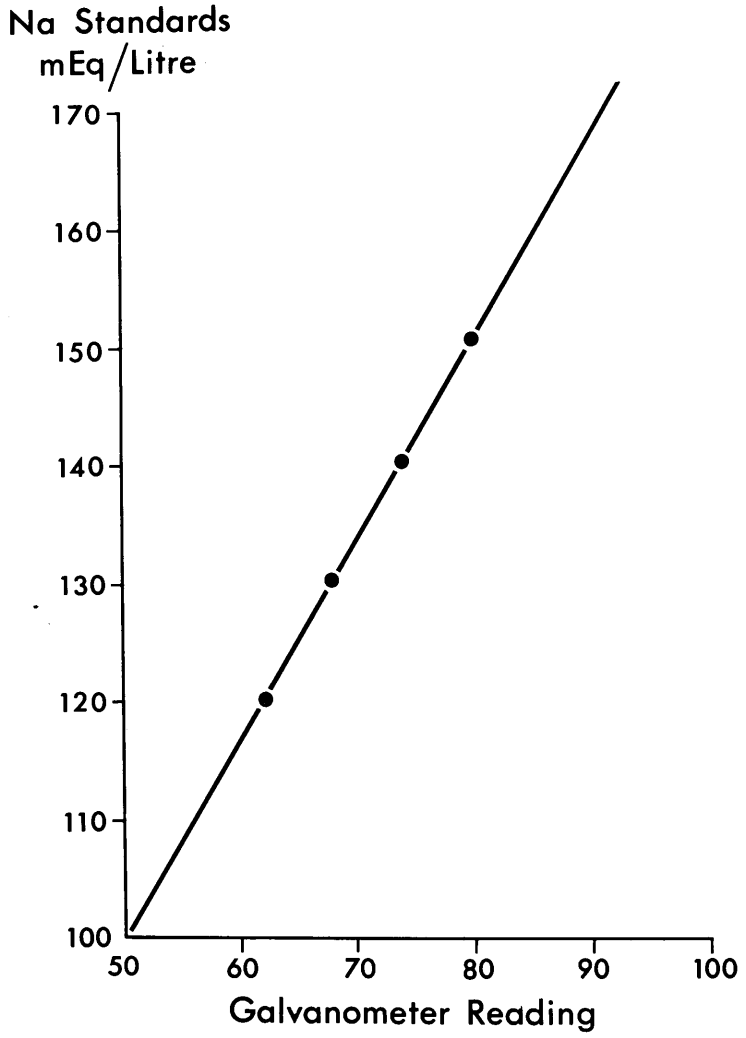


LABIAL MUCOUS GLANDS

Photomicrograph showing normal appearances

(A) Magnification x 75 (B) Magnification x 190

FIGURE I, 45



ESTIMATION OF SALIVARY SODIUM

- graph used to determine sodium values from standards.

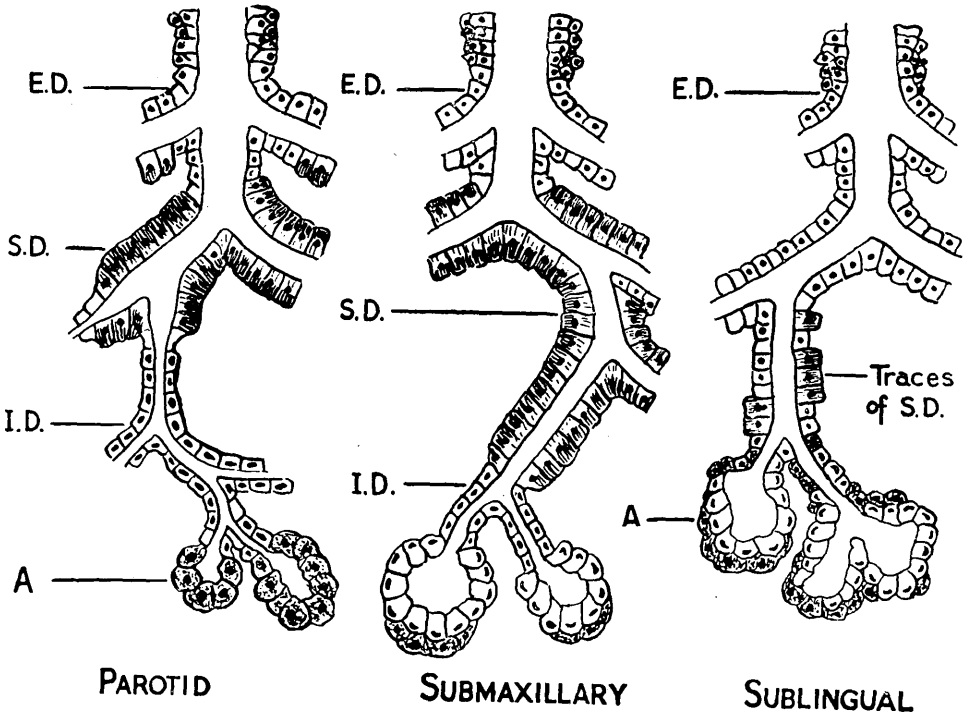
TABLE II, 1

NORMAL VALUES FOR SOME CONSTITUENTS OF PAROTID SALIVA

CONSTITUENT	LOW FLOW RATES (< 0.2 ml/min.)					HIGH FLOW RATES (> 0.5 ml/min.)				
	MEAN	RANGE	S.D.	S.E.	REFERENCE	MEAN	RANGE	S.D.	S.E.	REFERENCE
Sodium (mEq/l)	2.61	-	2.00	-	Shannon (1966) *	-	25-90	-	-	Hildes (1955) *
	6.9	2.4-14.3		1.3	Chapt. 12 *	64.8	43.5 -82.1	-	3.1	Chapt. 12 *
Potassium (mEq/l)	36.68		12.51	-	Shannon (1966) *	-	18-35	-	-	Hildes (1955) *
	20.4	15.2-26.0		1.1	Chapt. 12 *	20.9	16.8 -26.0	-	0.8	Chapt. 12 *
Chloride (mEq/l)	24.78	-	7.64	-	Shannon (1966) *					
	20.7	14.3-25.4	-	0.9	Chapt. 12 *	32.7	25.3 -49.2	-	2.3	Chapt. 12 *
Bicarb. (mEq/l)	1.04	-	0.96	-	Shannon (1966)					
	-	16 - 35	-	-	Thaysen et al (1954)	-	40 - 65	-	-	Thaysen et al (1954)
Calcium (mg%)	6.04	-	2.00	-	Shannon (1966)	3.5	2.1 - 6.7	1.4	-	Mandel et al (1964)
Inorganic Phosphate (mg%)	31.58	-	14.61	-	Shannon (1966)	11.1	7.0 -16.5	2.8		Mandel et al (1964)
Total Protein (mg%)	234.6	-	40.4	-	Shannon (1966)	190	100-366	68.9	-	Mandel et al (1964)
Uric Acid (mg%)	9.52	-	4.24	-	Shannon (1966) *					
	4.0	3.1-5.2	-	0.43	Chapt. 13 *	1.7	1.1 - 2.7	-	0.28	Chapt. 13 *

* Chapter numbers refer to the present studies.

FIGURE II, 1



THE SALIVARY GLAND DUCT SYSTEM - DIAGRAMATIC REPRESENTATION (AFTER JENKINS 1966)

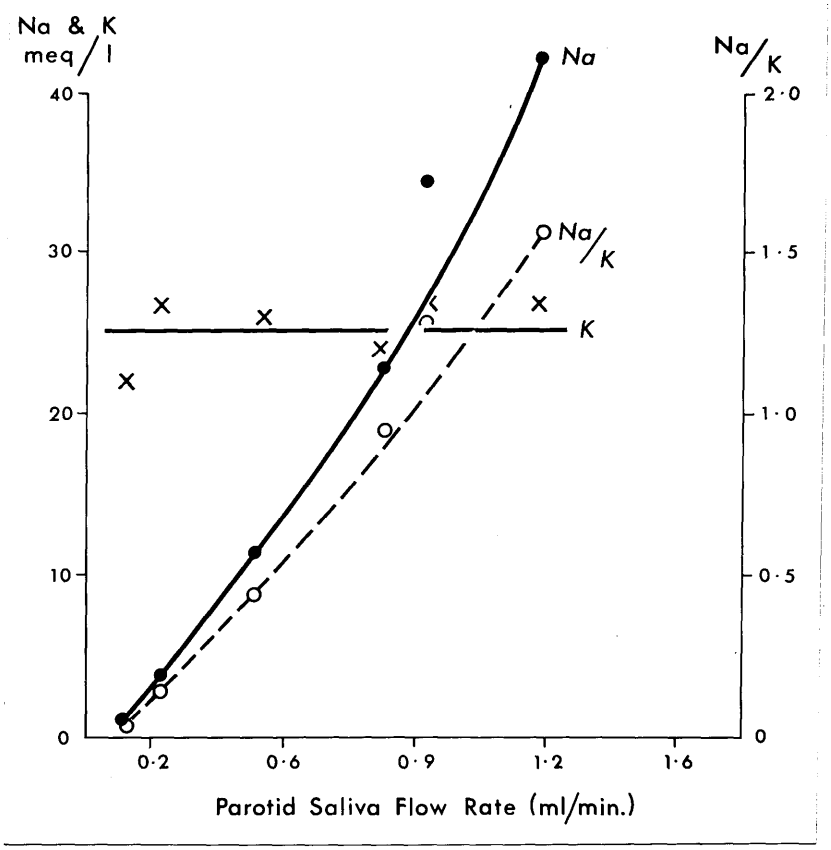
The ACINI (A) lead into the narrow INTERCALATED DUCTS (I.D.) lined by small cuboidal epithelial cells. These cells have a scanty cytoplasm which shows no striations. The intercalated ducts are short and not conspicuous in histological sections.

The 'STRIATED' DUCTS (S.D.) are intralobular ducts which are lined by taller dense-looking cells having a markedly striated appearance in their basal one-third. This duct area is thought to be most active in modifying the composition of saliva.

The EXCRETORY DUCTS (E.D.) are lined by two layered epithelium: a columnar superficial layer and a flattened deep layer. Near their termination an abrupt change to a multi-layered stratified squamous epithelium occurs.

N.B. The above description refers to parotid and submandibular glands only. The sublingual glands have no intercalated ducts and few striated ducts.

FIGURE II, 2



SODIUM AND POTASSIUM CONCENTRATIONS AND SODIUM/POTASSIUM RATIOS AT VARYING SALIVARY FLOW RATES IN PAROTID SALIVA.

TABLE II, 2

RELATION BETWEEN PLASMA IODIDE AND PAROTID SALIVARY IODIDE CONCENTRATION IN A NORMAL SUBJECT GIVEN IODIDE SUPPLEMENTS

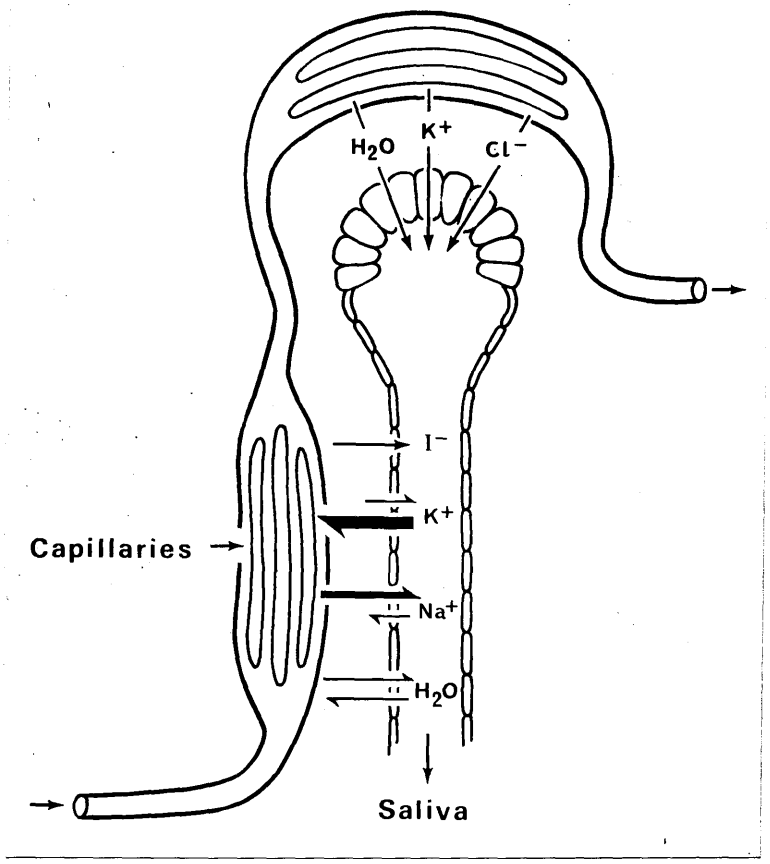
Plasma inorganic iodide (µg/100ml)	Saliva iodide (µg/100ml)	Saliva/plasma iodide ratio
0.30	4.9	16.4
0.56	10.8	19.4
2.30	56.0	24.1
25.90	555.0	21.4

TABLE II , 3

COMPARISON OF PAROTID SODIUM, POTASSIUM, AND CHLORIDE CONCENTRATION (m.eq./l.)
AT DIFFERENT FLOW RATES IN 10 NORMAL SUBJECTS

SUBJECT	AGE	SEX	'RESTING'			FLOW RATE (Vol/min.)	FRUIT GUM STIMULATION			FLOW RATE (Vol/min.)	LEMON JUICE STIMULATION			FLOW RATE (Vol/min.)
			Na.	K.	Cl.		Na.	K.	Cl.		Na.	K.	Cl.	
1	40	F	3.2	22.4	20.2	0.12	22.0	20.3	18.2	0.42	72.3	19.0	30.1	1.32
2	53	F	12.0	19.7	24.3	0.15	15.0	18.5	16.8	0.40	43.5	26.0	28.2	1.13
3	43	F	4.1	18.3	20.2	0.11	13.9	23.2	21.4	0.35	61.9	20.0	29.1	1.30
4	65	M	6.4	16.4	14.3	0.13	9.0	15.3	23.4	0.53	82.1	16.8	25.3	1.35
5	46	M	3.8	24.6	19.6	0.09	11.2	27.3	14.0	0.26	69.7	21.4	37.3	1.63
6	59	F	3.0	23.2	21.3	0.13	21.6	23.0	27.5	0.30	65.3	20.8	43.0	1.54
7	39	M	11.5	26.0	19.9	0.11	32.0	22.0	26.0	0.41	68.2	24.0	30.2	0.94
8	48	F	14.3	21.8	23.2	0.10	15.0	20.5	18.6	0.39	59.3	21.3	26.3	0.89
9	37	M	8.9	16.4	25.4	0.08	9.1	25.9	35.3	0.62	61.9	20.3	49.2	1.68
10	22	M	2.4	15.2	19.3	0.05	9.4	17.6	15.0	0.18	63.8	20.0	29.0	1.38
RANGE	22-65		2.4-14.3	15.2-26.0	14.3-25.4	0.05-0.15	9.0-32.0	15.3-27.3	14.0-35.3	0.18-0.62	43.5-82.1	16.8-26.0	25.3-49.2	0.89-1.68
MEAN	45.2		6.9	20.4	20.7	0.10	15.8	21.3	21.6	0.39	64.8	20.9	32.7	1.32
S.E.M.	3.84		1.3	1.1	0.9	0.01	2.3	1.1	2.0	0.04	3.1	0.8	2.3	0.08

FIGURE II, 3



DIAGRAMATIC REPRESENTATION OF POSSIBLE MECHANISMS UNDERLYING CHANGES IN CONCENTRATION OF SALIVARY CONSTITUENTS WITH VARIATION IN FLOW RATE.

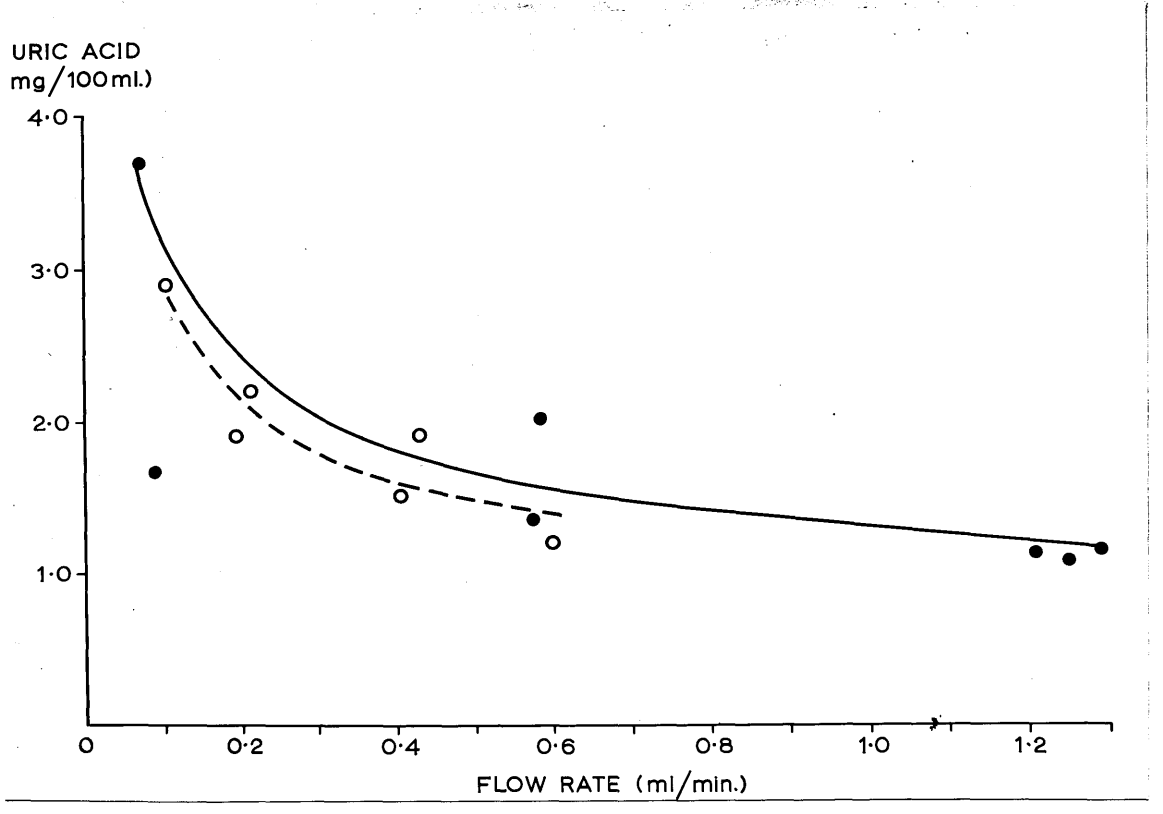
(After Davenport 1961).

TABLE II , 4

SALIVARY FLOW RATE UNSTIMULATED AND AFTER STIMULATION

	PAROTID SALIVA				SUBMANDIBULAR SALIVA			
Stimulus	No. of Patients	No. of Observations	Flow rate (ml/min) Mean	S.E.	No. of Patients	No. of Observations	Flow rate (ml/min) Mean	S.E.
Unstimulated	5	7	0.15	0.03	4	5	0.13	0.01
Salt	5	5	0.18	0.04	4	4	0.36	0.09
Paraffin Wax	5	5	0.48	0.13	4	3	0.31	0.07
Fruit Gum	5	5	0.75	0.15	4	6	0.73	0.06
Oxo	4	4	0.79	0.18	2	2	0.46	0.08
Lemon Juice	5	8	1.08	0.22	4	6	0.96	0.17

FIGURE II, 4

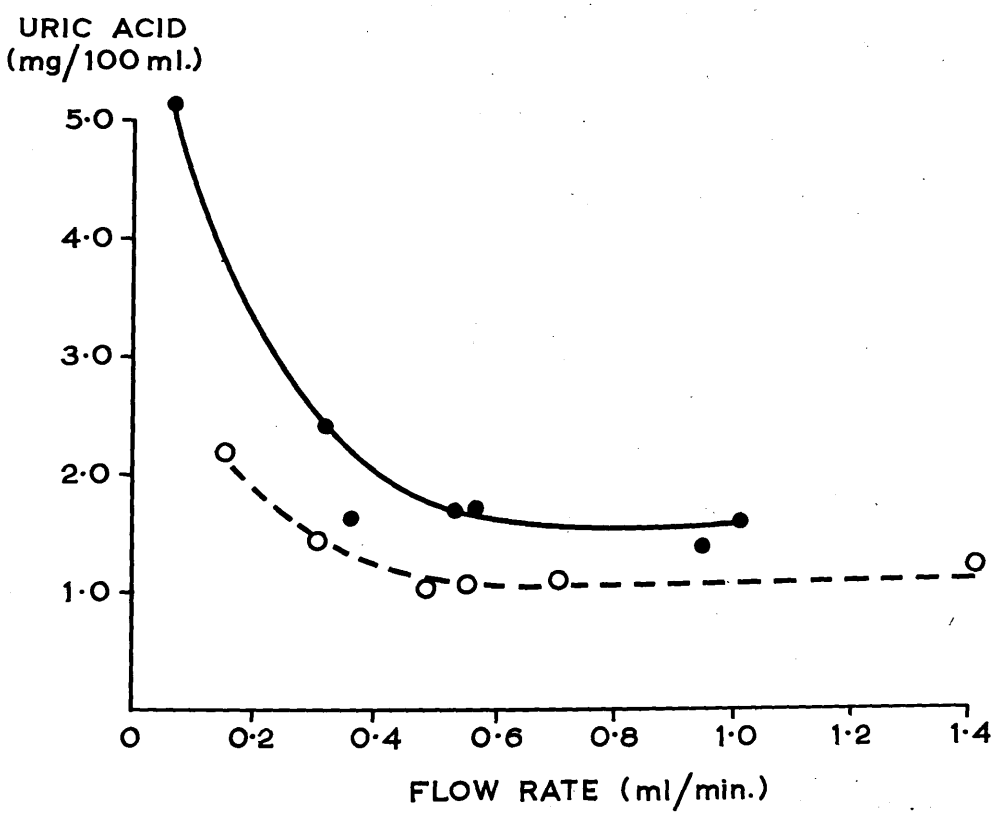


RELATION BETWEEN SALIVARY FLOW RATE AND URIC ACID CONCENTRATION IN SUBJECT 1.

● ———— ● Parotid saliva

0 ---------- 0 Submandibular saliva

FIGURE II, 5

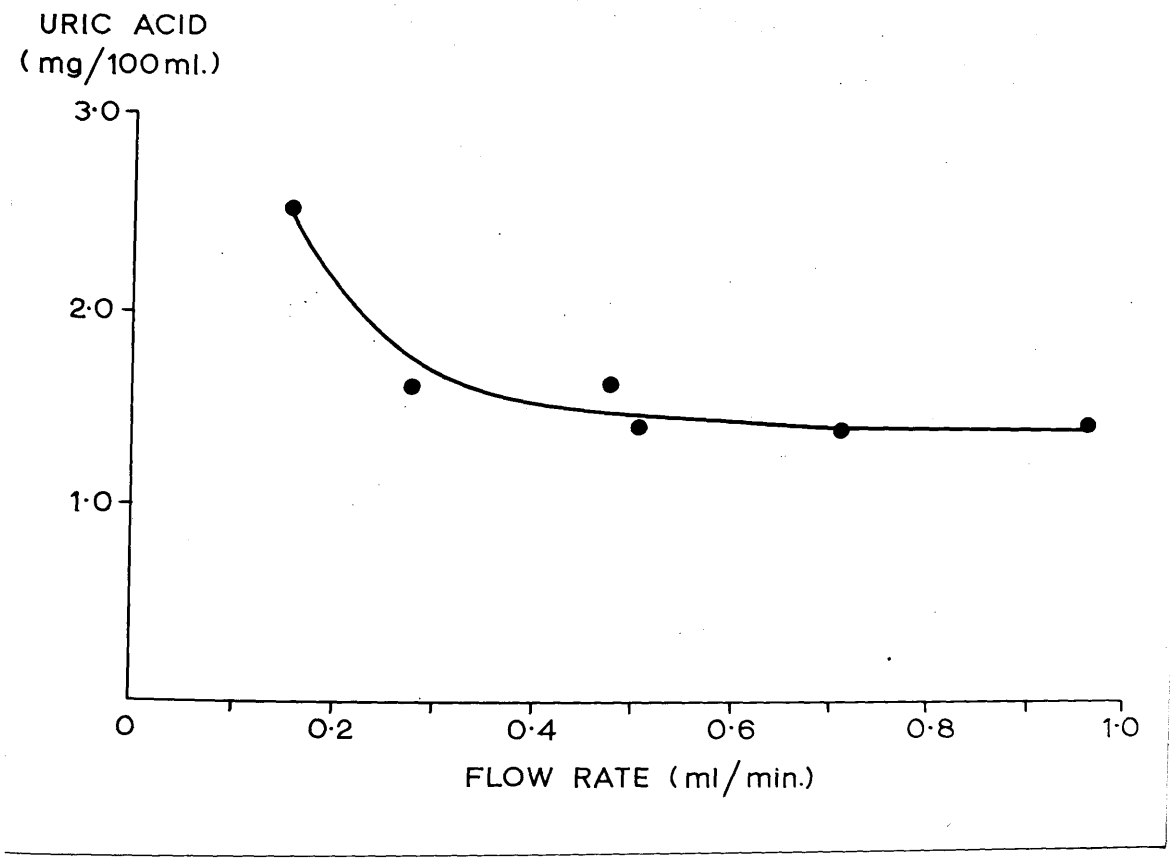


RELATION BETWEEN SALIVARY FLOW RATE AND URIC ACID CONCENTRATION IN SUBJECT 2

●——— Parotid saliva

0------0 Submandibular saliva

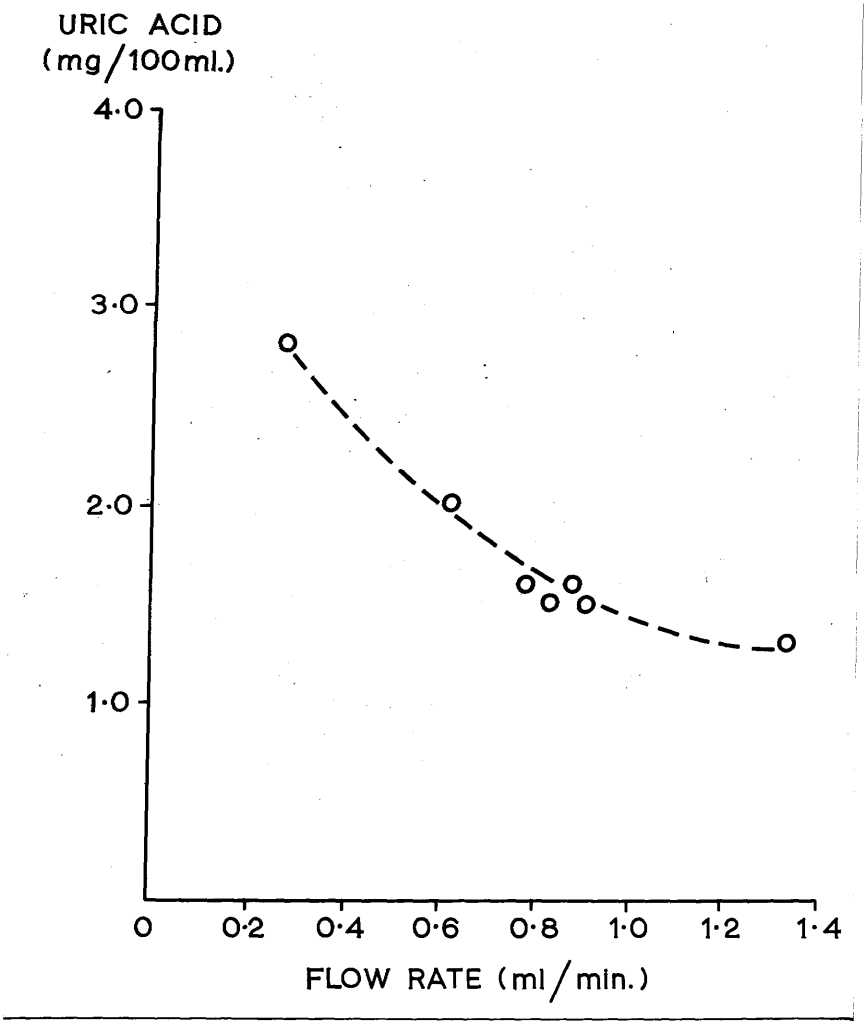
FIGURE II, 6



RELATION BETWEEN SALIVARY FLOW RATE AND URIC ACID CONCENTRATION IN SUBJECT 3.

●——● Parotid saliva

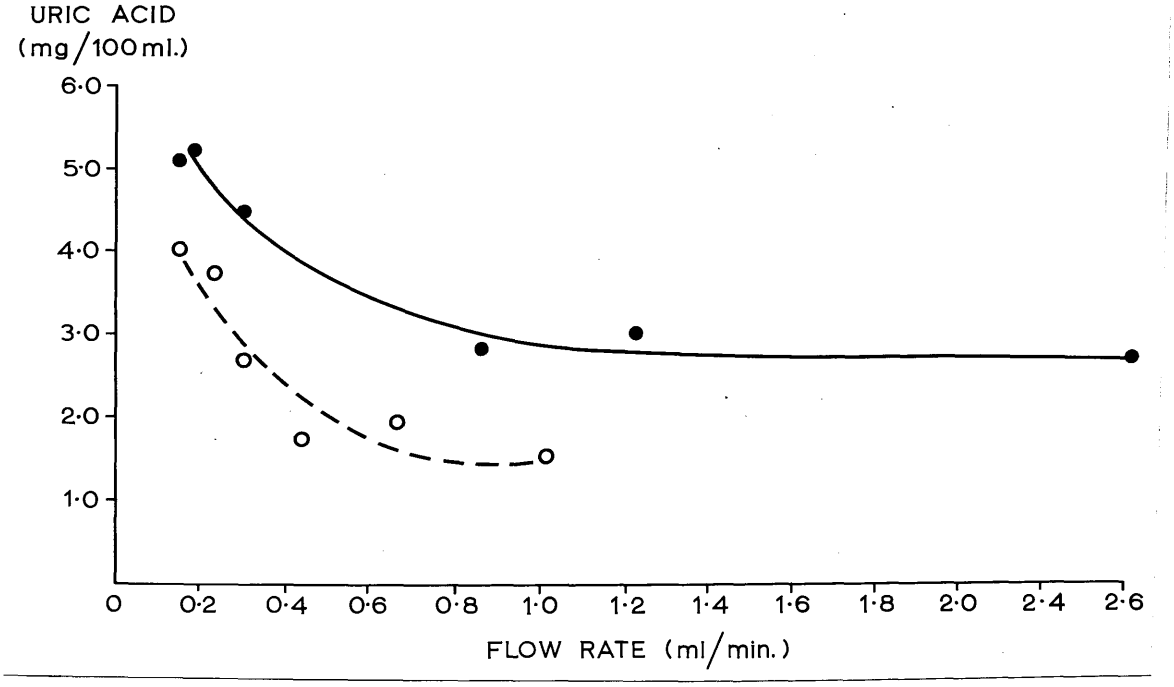
FIGURE II, 7



RELATION BETWEEN SALIVARY FLOW RATE AND URIC ACID CONCENTRATION IN SUBJECT 4

o--------o Submandibular saliva

FIGURE II , 8

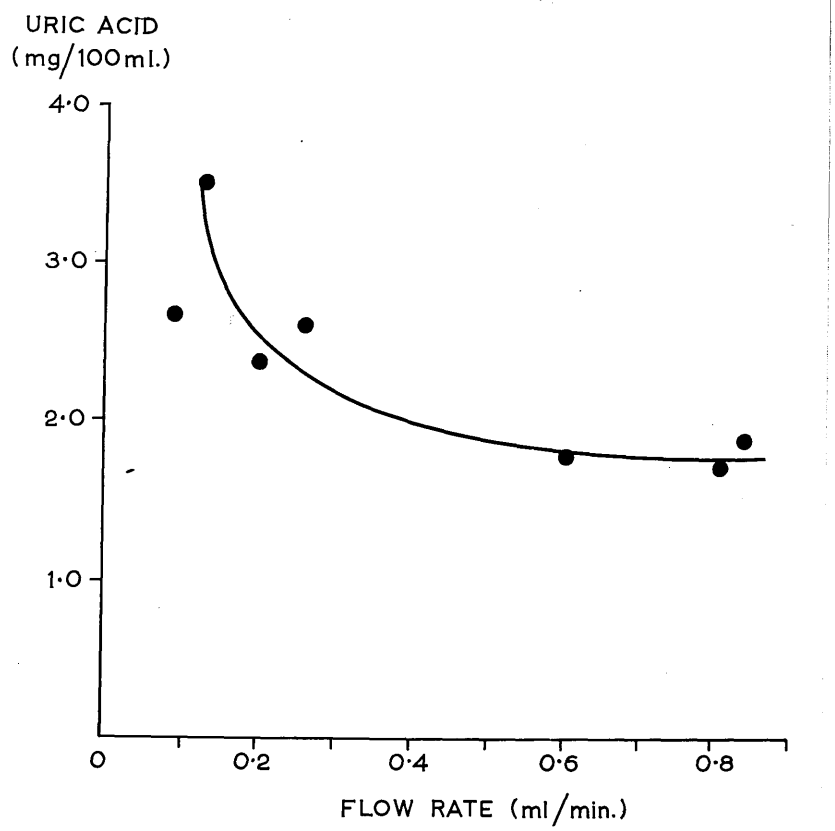


RELATION BETWEEN SALIVARY FLOW RATE AND URIC ACID CONCENTRATION IN SUBJECT 5.

●——● Parotid saliva

0------0 Submandibular saliva

FIGURE II, 9



RELATION BETWEEN SALIVARY FLOW RATE AND URIC ACID CONCENTRATION IN SUBJECT 6

●——● Parotid saliva

TABLE II , 5

URIC ACID CONCENTRATION IN SERUM AND PAROTID AND SUBMANDIBULAR SALIVA

SUBJECT	PAROTID SALIVA - URIC ACID					SUBMANDIBULAR SALIVA - URIC ACID			
	SERUM URIC ACID mg%	LOW FLOW RATES mg%	LOW FLOW RATES mg/hr	STIMU-LATED mg%	STIMU-LATED mg/hr	LOW FLOW RATES mg%	LOW FLOW RATES mg/hr	STIMU-LATED mg%	STIMU-LATED mg/hr.
1	4.0	3.7	0.15	1.1	0.66	2.9	0.17	1.2	0.72
2	3.5	5.1	0.15	1.4	0.84	2.1	0.18	1.0	0.60
3	3.2	3.1	0.25	1.7	1.02	-	-	-	-
4	4.1	-	-	-	-	4.0	0.02	1.5	0.90
5	4.8	5.2	0.56	2.7	1.62	4.0	0.36	1.5	0.90
6	3.3	3.1	0.24	1.4	0.84	-	-	-	-
MEAN	3.8	4.0	0.27	1.7	0.99	3.3	0.18	1.3	0.78
S.E.	0.25	0.43	0.07	0.28	0.17	0.46	0.07	0.12	0.07

TABLE II , 6

CORRELATION COEFFICIENTS BETWEEN LOG (VOL/MIN) AND LOG (URIC ACID CONCENTRATION). THE SHAPE OF THE REGRESSION LINES ARE NOT SIGNIFICANTLY DIFFERENT FROM EACH OTHER

Subject	PAROTID SALIVA			SUBMANDIBULAR SALIVA		
	No. of Observations	r.	P.	No. of Observations	r	P.
1	7	- 0.80	< 0.05	6	- 0.91	$\doteqdot$ 0.01
2	7	- 0.95	< 0.01	6	- 0.76	$\doteqdot$ 0.08
3	7	- 0.80	< 0.05	-	-	-
4	-	-	-	8	- 0.93	$<$ 0.01
5	6	- 0.96	< 0.01	6	- 0.92	$<$ 0.01
6	7	- 0.91	< 0.01	-	-	-

TABLE II, 7

CARBONIC ANHYDRASE ACTIVITY IN SALIVA IMMEDIATELY AFTER COLLECTION AND AFTER STORING FOR 24 AND 48 HOURS AT 0°C

	CARBONIC ANHYDRASE ACTIVITY (K/ml)		
SAMPLE NO.	ON COLLECTION	AFTER 24 HOURS	AFTER 48 HOURS
1	2.02	2.04	2.02
2	2.07	2.06	2.04
3	2.00	1.97	2.00
4	2.07	2.02	2.09

TABLE II, 8

CARBONIC ANHYDRASE ACTIVITY IN SALIVA IMMEDIATELY AFTER COLLECTION AND AFTER 24 AND 48 HOURS AT ROOM TEMPERATURE

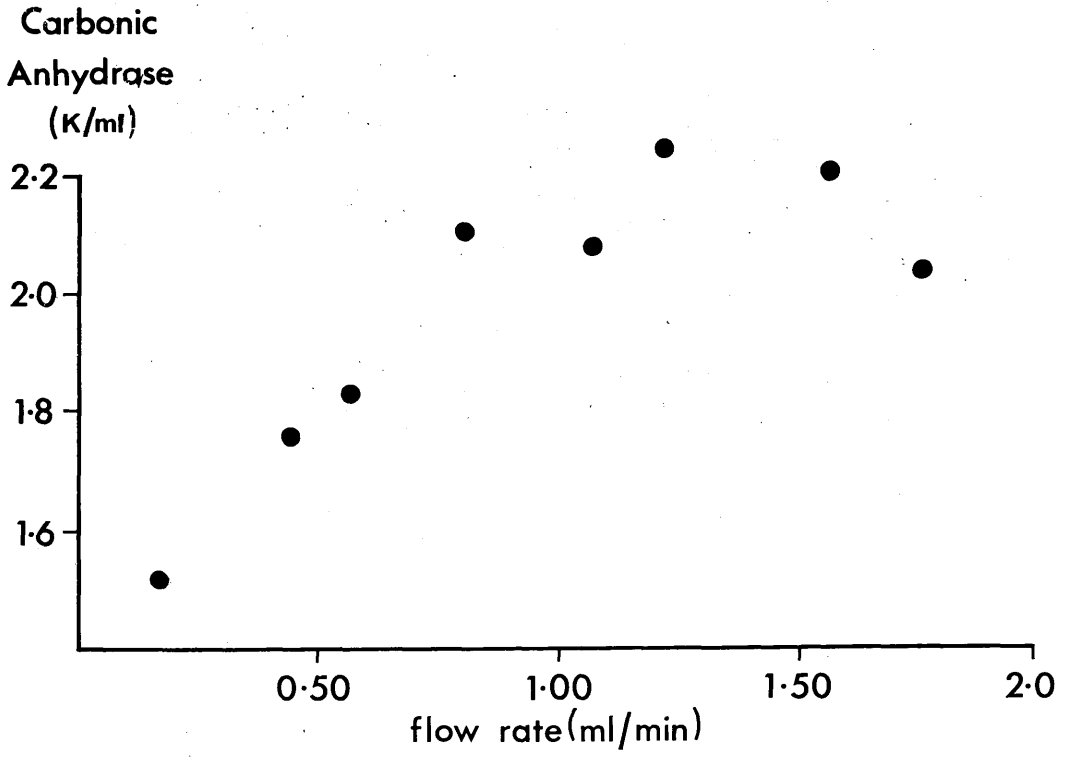
	CARBONIC ANHYDRASE ACTIVITY (K/ml)		
SAMPLE NO.	ON COLLECTION	AFTER 24 HOURS	AFTER 48 HOURS
1	1.77		1.77
2	1.84		1.95
3	2.02		2.05
4	2.07		2.07
5	1.92	1.95	1.92
6	1.87	1.90	1.87
7	2.02	2.00	2.00

TABLE II, 9

CARBONIC ANHYDRASE ACTIVITY IN SALIVA COLLECTED WITHOUT OIL AND UNDER OIL, IMMEDIATELY AFTER COLLECTION AND AFTER 48 HOURS AT 37°C

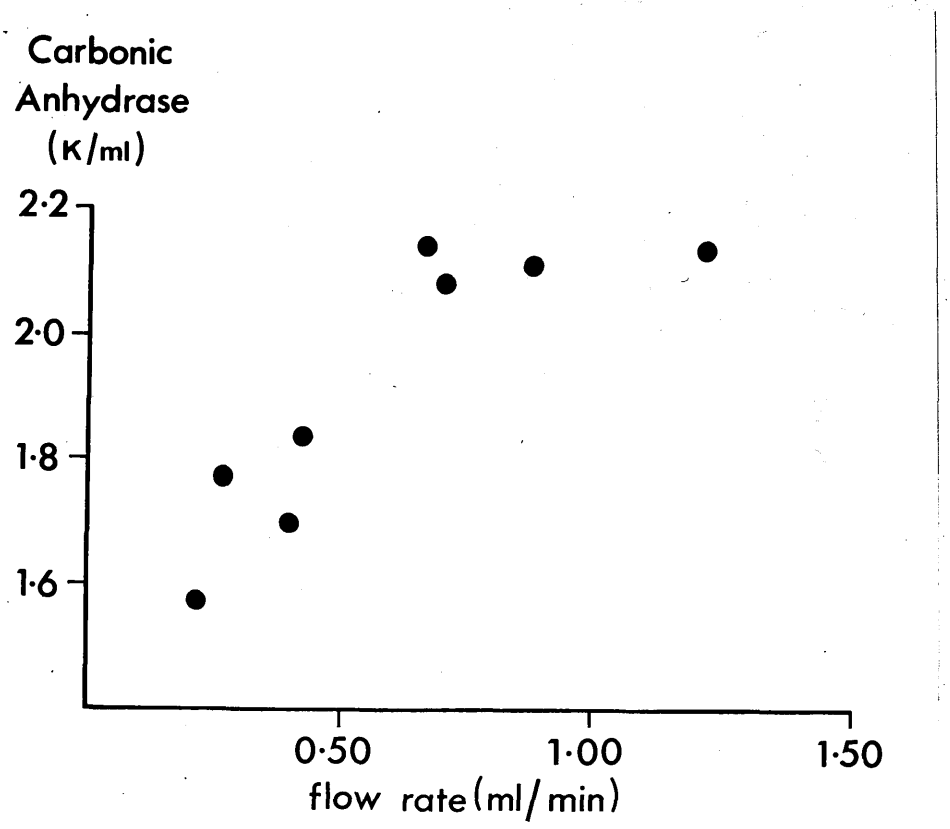
K/ml				
Sample	Without oil		Under oil	
No.	On Collection	After 48 hours	On Collection	After 48 hours
1	2.02	2.02	2.02	2.06
2	2.14	2.06	2.14	2.09
3	1.95	1.97	2.02	2.00
4	2.04	2.04	2.06	2.04
5	1.97	1.97	2.02	2.02
6	2.02	2.02	2.02	2.02

FIGURE II, 10



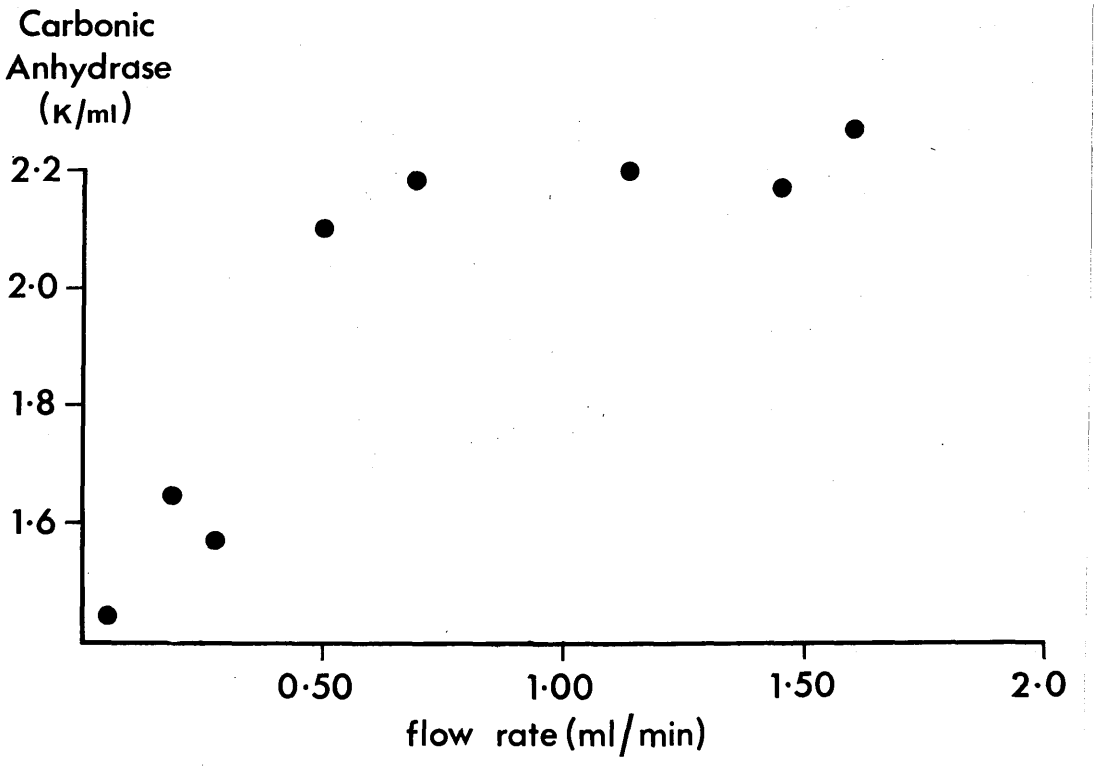
CARBONIC ANHYDRASE ACTIVITY IN PAROTID SALIVA SECRETED AT DIFFERENT FLOW RATES IN SUBJECT 1.

FIGURE II, 11



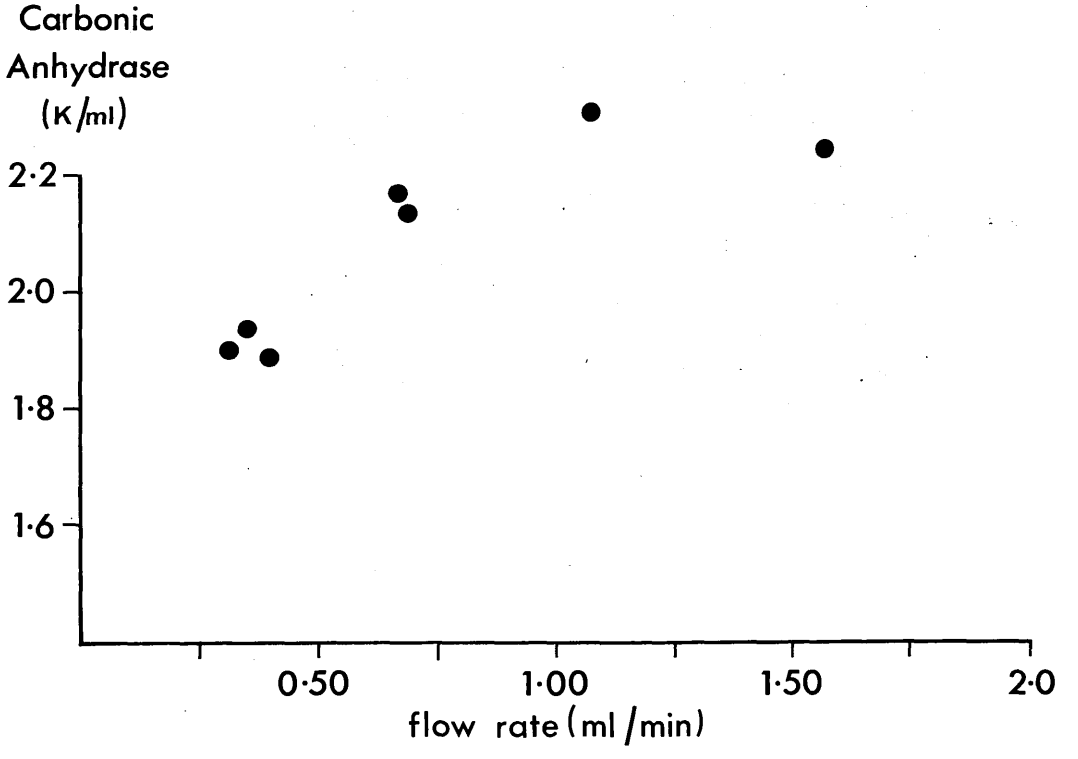
CARBONIC ANHYDRASE ACTIVITY IN PAROTID SALIVA SECRETED AT DIFFERENT FLOW RATES IN SUBJECT 2.

FIGURE II, 12



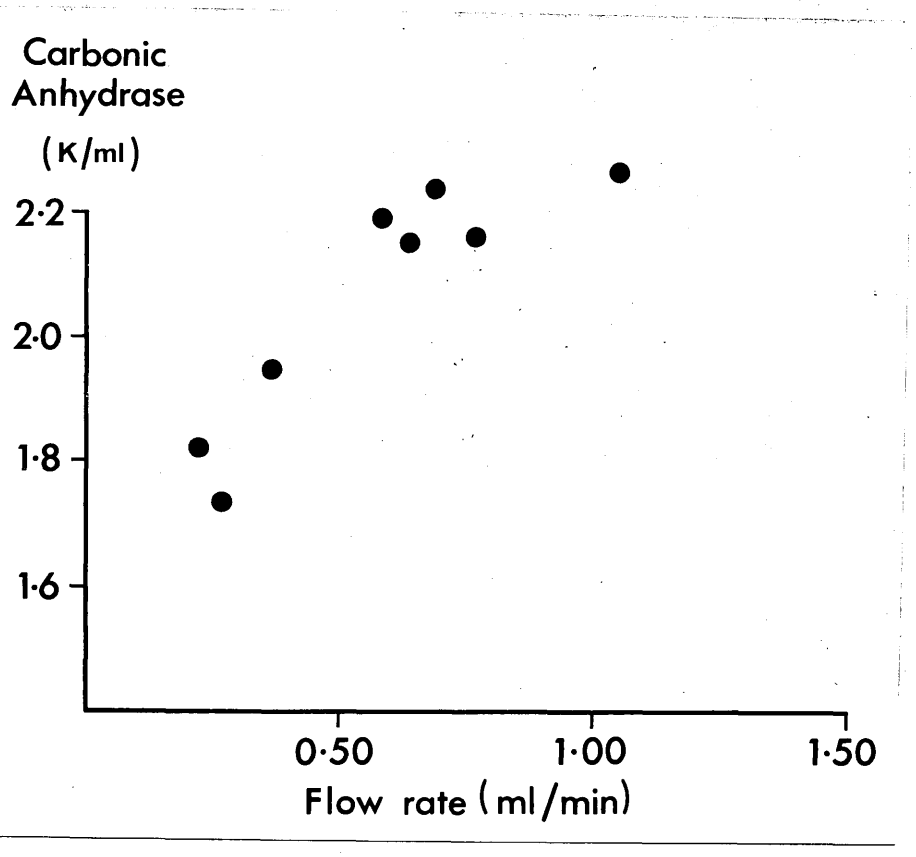
CARBONIC ANHYDRASE ACTIVITY IN PAROTID SALIVA SECRETED AT DIFFERENT FLOW RATES IN SUBJECT 3.

FIGURE II , 13



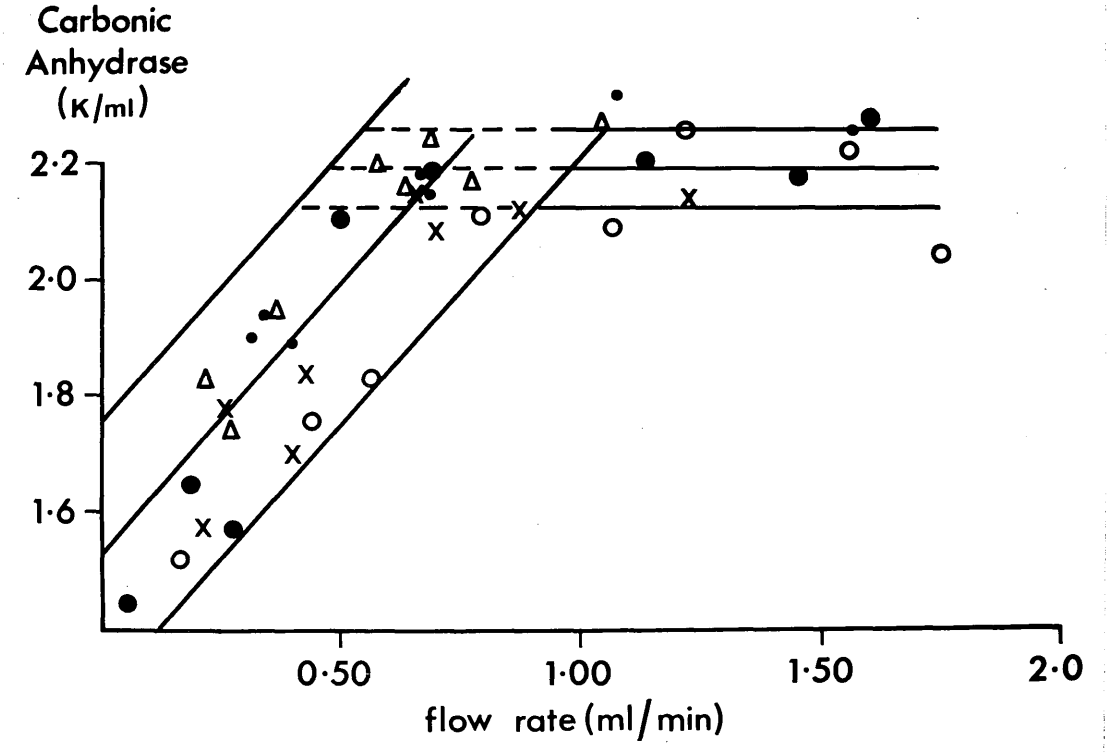
CARBONIC ANHYDRAS ACTIVITY IN PAROTID SALIVA SECRETED AT DIFFERENT FLOW RATES IN SUBJECT 4.

FIGURE II, 14



CARBONIC ANHYDRASE ACTIVITY IN PAROTID SALIVA SECRETED AT DIFFERENT FLOW RATES IN SUBJECT 5.

FIGURE II, 15



CARBONIC ANHYDRASE ACTIVITY IN PAROTID SALIVA SECRETED AT DIFFERENT FLOW RATES IN THE FIVE SUBJECTS.

TABLE II, 10

CARBONIC ANHYDRASE ACTIVITY IN STIMULATED PAROTID SUBMANDIBULAR AND MIXED SALIVA OF 2 SUBJECTS ON 3 CONSECUTIVE DAYS

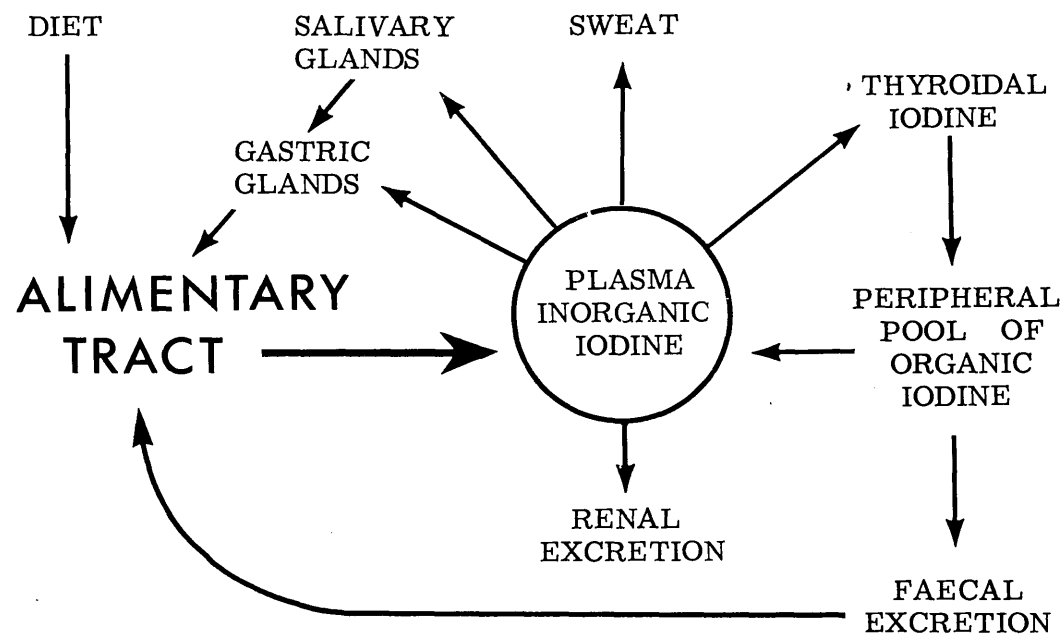
		Carbonic anhydrase activity (K/ml)	
		Subject 1	Subject 2
Parotid* Saliva	Day 1	2.18	2.07
	Day 2	2.19	2.03
	Day 3	2.18	2.13
	Mean	2.18	2.08
Submandibular* Saliva	Day 1	2.00	2.04
	Day 2	2.06	2.00
	Day 3	2.13	2.00
	Mean	2.06	2.01
Mixed Saliva +	Day 1	2.13	2.12
	Day 2	2.11	2.01
	Day 3	2.12	2.17
	Mean	2.12	2.10
Blood		1.87	1.88

* Lemon Juice Stimulation

\+ Paraffin Wax "

PART III

FIGURE III , 1



OUTLINE OF IODINE METABOLISM

Iodine is absorbed from the alimentary tract into the plasma inorganic iodine pool. Some is excreted by the kidneys and some is taken up by the thyroid, salivary and gastric glands, and some by skin and hair. In the thyroid gland iodine is converted to thyroid hormone by organification and thyroxine is secreted from the thyroidal iodine pool into the peripheral pool of organic iodine. The latter is made up of thyroid hormones in the plasma and tissues. Part of the iodine leaves this pool in the faeces but most is deiodinated and re-enters the plasma inorganic iodine pool. The iodine concentrated by the salivary glands is only in the inorganic form and it is reabsorbed from the small intestine following ingestion. These cycles are repeated.

TABLE III, 1

NORMAL VALUES OF THE PLASMA INORGANIC IODINE (PII) IN µg/100 ml (After Wayne et al 1964)

	Mean	Range	S.D.	S.E.
Feinberg et al (1959)	0.28	0.10-0.43		
Perry & Hughes (1952)	0.17			0.005
*Reilly et al (1958)	0.55			0.06
*Wagner et al (1961)	0.50		0.30	
Zingg & Perry (1953)	0.23			0.06
Beckers (1962)	0.26		0.09	0.028
Wayne et al (1964)	0.18	0.04-0.57	0.10	0.015

* U.S.A. series

TABLE III, 2

EXTRATHYROIDAL IODIDE-CONCENTRATING TISSUES OF CHORDATES

TISSUE	SPECIES, ETC.	COMMENTS	REFERENCE
Salivary glands			
Parotid -	Man, dog, guinea pig	Concentrated by duct cells	Cohen and Myant (1959)
Submandibular -	Man, mouse, Hamster, Guinea pig		Brown - Grant (1961)
Sublingual -	Cat, Rabbit		
All -	Negligible in rat		
Stomach	All vertebrates investigated	Concentrated by mucous cells; independent of HCl secretion	Myant et al (1950) Honour et al (1952)
Small intestine	Rat		Pastan (1957)
Mammary gland	All species investigated	Some organic iodine in certain species; sizable I loss from body	Brown - Grant (1957)
Uterus	Rat	Endometrium	Brown - Grant (1965)
Ovary or ova	Hen, amphibia, teleosts, cyclostomes		Leloup and Fontaine (1960)
Placenta	Rabbit, guinea pig, ? rat	Hemoendothelial placentas	Logothetopoulos and Scott (1955)
Notochord	Cyclostomes	$I^- > Br^- > Cl^-$	Leloup (1952)
Epidermis and hair	Rat, Rana		Leblond (1954) Brown - Grant (1961)
Gills	Scyllium		Le Loup and Fontaine (1960)
Serum	Migratory teleosts: Salmo, Alosa, Mugil	Bound to "albumin"	
Ciliary body-iris	Rabbit	Anion behaviour like that in thyroid	Becker (1961 a)
Choroid plexus	Rabbit		Becker (1961 b)
Nasal gland	Herring gull	$Cl^- > I^-$	Carey (1962)

TABLE III, 3

S : P ^{131}I concentration ratios for mixed saliva and for saliva from separate salivary glands of ten species (Cohen and Myant - 1959)

Species	Mixed	Parotid	Submandibular	Sublingual	Residual
Cat	+ +	0	0	+	+ +
Dog	+ + +	+ + +	0 to +	0 to +	+ to + +
Rabbit	+	+	–	–	+
Guinea-pig	+ + +	+ + +	+	+	+
Cotton-rat	+ + +	+ +	+ +	+ +	+
Rat	0	0	0	0	+
Mouse	+ + +	+	+ + +	0	0
Hamster	+ + +	+	+ + +	0	+
Mastomys	+ +	–	+ +	–	–
Man	+ + +	+ + +	+ + +	–	–

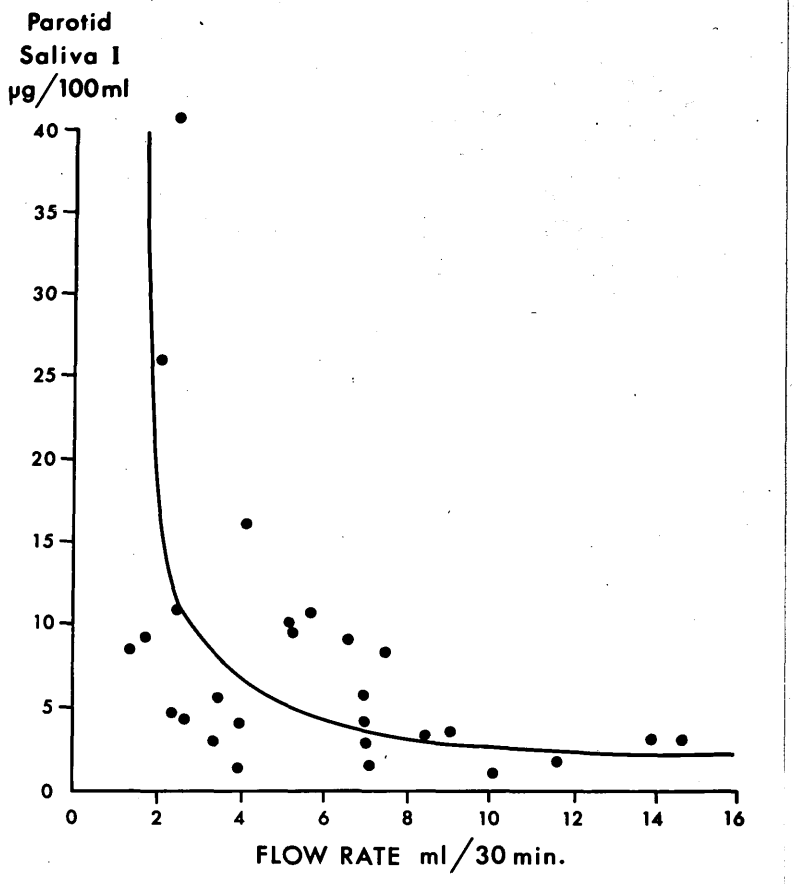
0 = < 1, + = 1-5, ++ = 5-10, +++ = > 10.

TABLE III, 4

SALIVARY FLOW RATES IN RESPONSE TO STIMULI

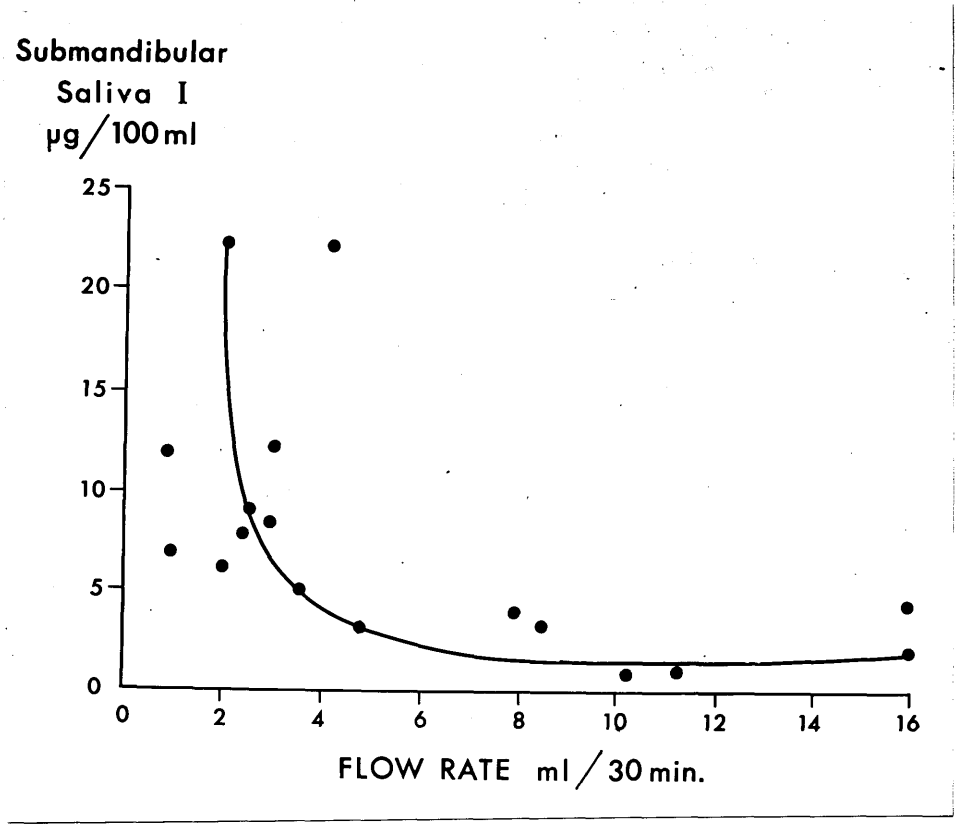
STIMULUS	PAROTID SALIVA				SUBMANDIBULAR SALIVA			
	No. of Patients	No. of Observ-ations	Flow rate (ml/min) Mean	S.E.	No. of Patients	No. of Observ-ations	Flow Rate (ml/min) Mean	S.E.
Resting	5	12	0.16	0.021	2	3	0.06	0.029
Salt	5	10	0.42	0.047	2	3	0.61	0.151
Paraffin Wax	5	5	0.47	0.076	3	4	0.34	0.074
Fruit Gum	5	15	0.88	0.136	3	7	0.75	0.06
Oxo	5	9	0.90	0.128	1	1	1.33	-
Lemon Juice	5	12	1.89	0.249	3	5	1.15	0.13

FIGURE III , 2



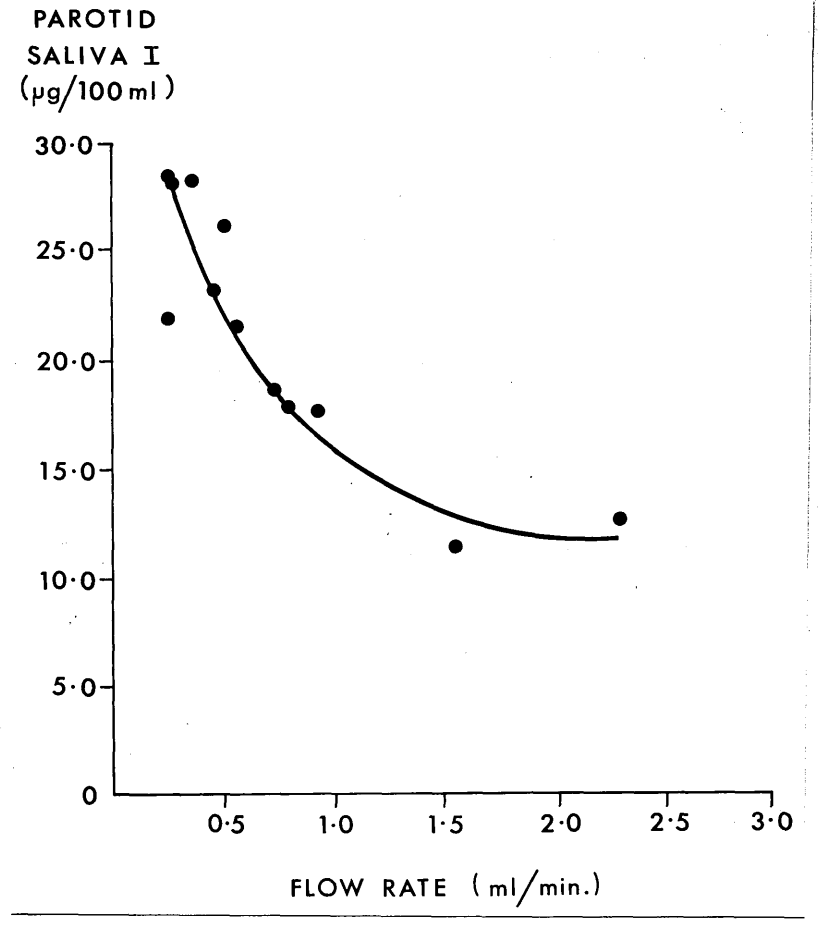
RELATION BETWEEN CONCENTRATION OF IODIDE IN PAROTID SALIVA AND FLOW RATE IN TWENTY-SEVEN SUBJECTS IN WHOM SALIVA WAS COLLECTED FOR 30 MINS.

FIGURE III, 3



RELATION BETWEEN CONCENTRATION OF IODIDE IN SUBMANDIBULAR SALIVA AND FLOW RATE IN SIXTEEN SUBJECTS IN WHOM SALIVA WAS COLLECTED FOR 30 MINS.

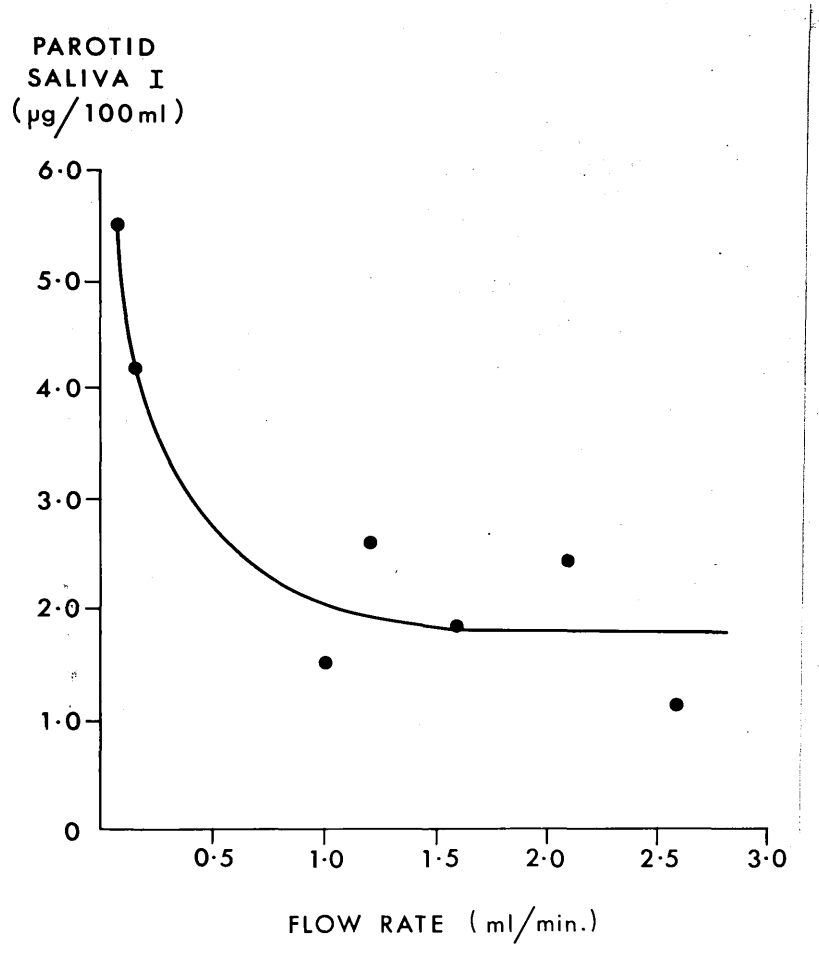
FIGURE III , 4



CONCENTRATION OF IODIDE IN PAROTID SALIVA OF ONE SUBJECT AT DIFFERENT FLOW RATES.

5% confidence limits for correlation coefficient
- .739 to -.978

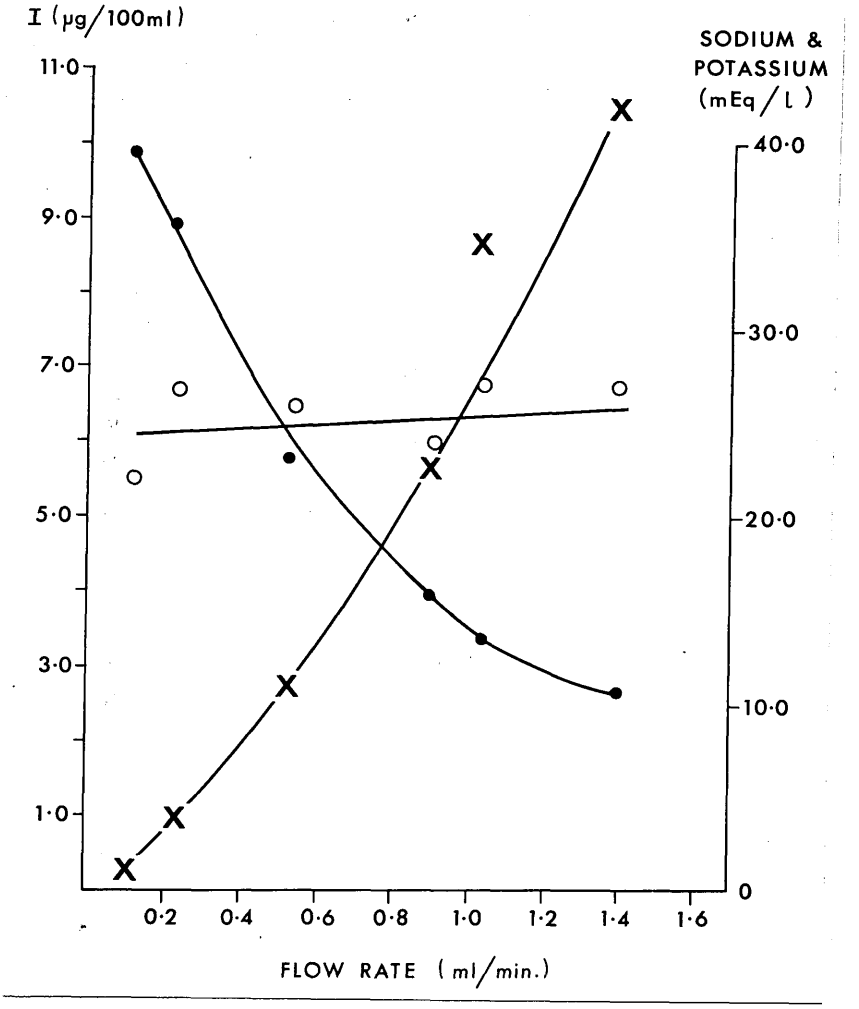
FIGURE III, 5



CONCENTRATION OF IODIDE IN PAROTID SALIVA OF A SECOND PATIENT AT DIFFERENT FLOW RATES.

5% confidence limits correlation coefficient
-.178 to - .973

FIGURE III, 6

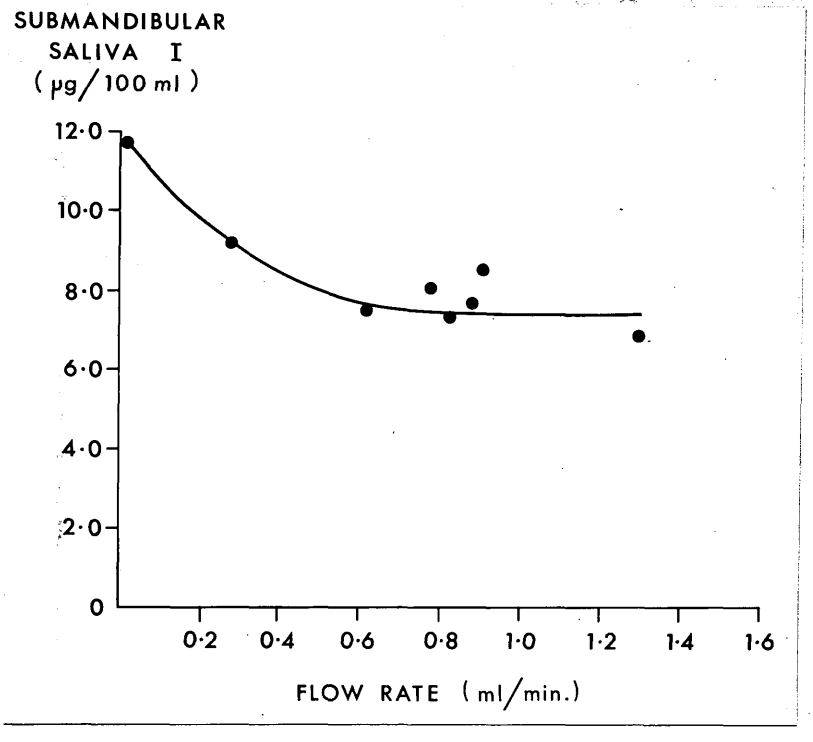


CONCENTRATION OF IODIDE, SODIUM AND POTASSIUM, IN PAROTID SALIVA COLLECTED FROM ONE PATIENT AT DIFFERENT FLOW RATES.

●——● iodide x——x sodium 0——0 potassium

5% confidence limits for correlation coefficient (iodide)
- .782 to - .995

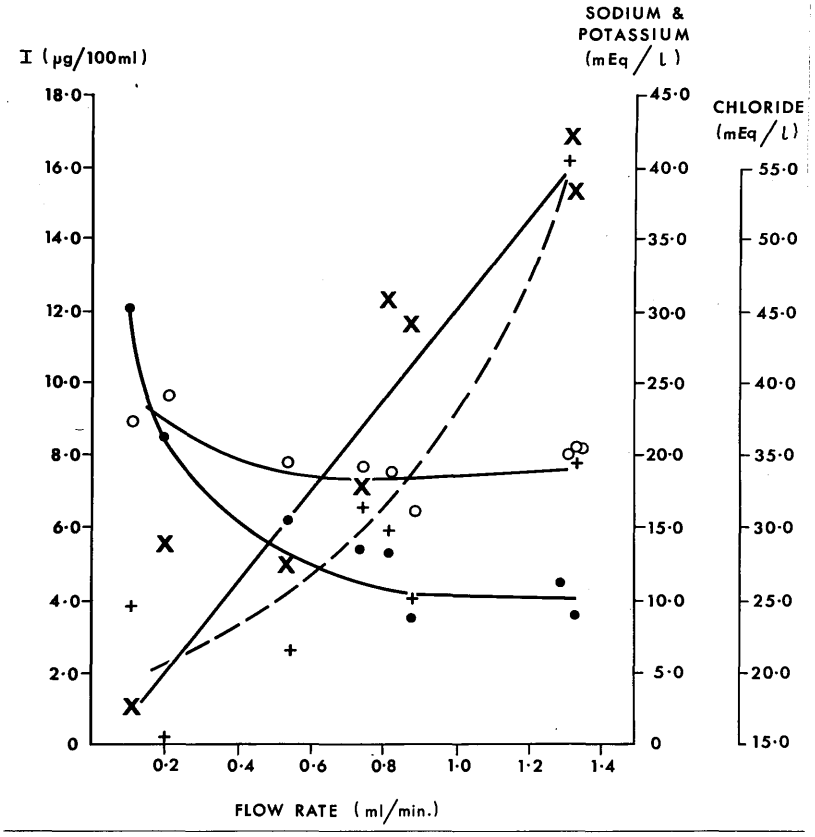
FIGURE III, 7



CONCENTRATION OF IODIDE IN SUBMANDIBULAR SALIVA OF ONE SUBJECT AT DIFFERENT FLOW RATES.

5% confidence limits for correlation coefficient -.772 to -.993

FIGURE III , 8



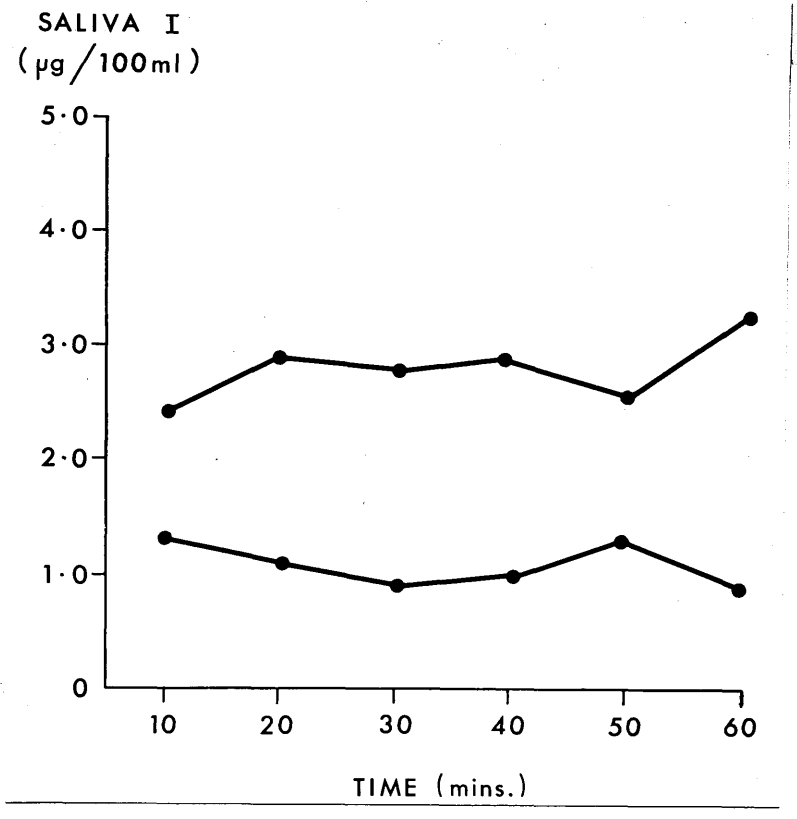
CONCENTRATION OF IODIDE, SODIUM, POTASSIUM AND CHLORIDE IN SUBMANDIBULAR SALIVA COLLECTED FROM ONE SUBJECT AT DIFFERENT FLOW RATES.

●——● iodide x ——— x sodium

0——— 0 potassium + ——— + chloride

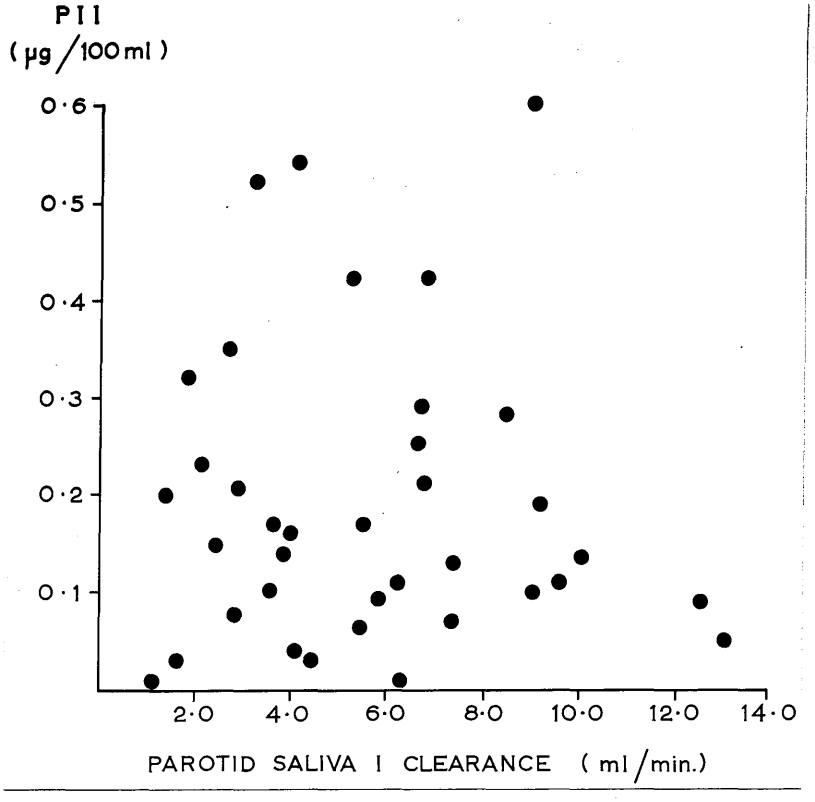
5% confidence limits for correlation coefficient (iodide)
- .380 to -.840

FIGURE III , 9



SALIVARY IODIDE CONCENTRATION IN TWO SUBJECTS AT CONSTANT FLOW RATES.

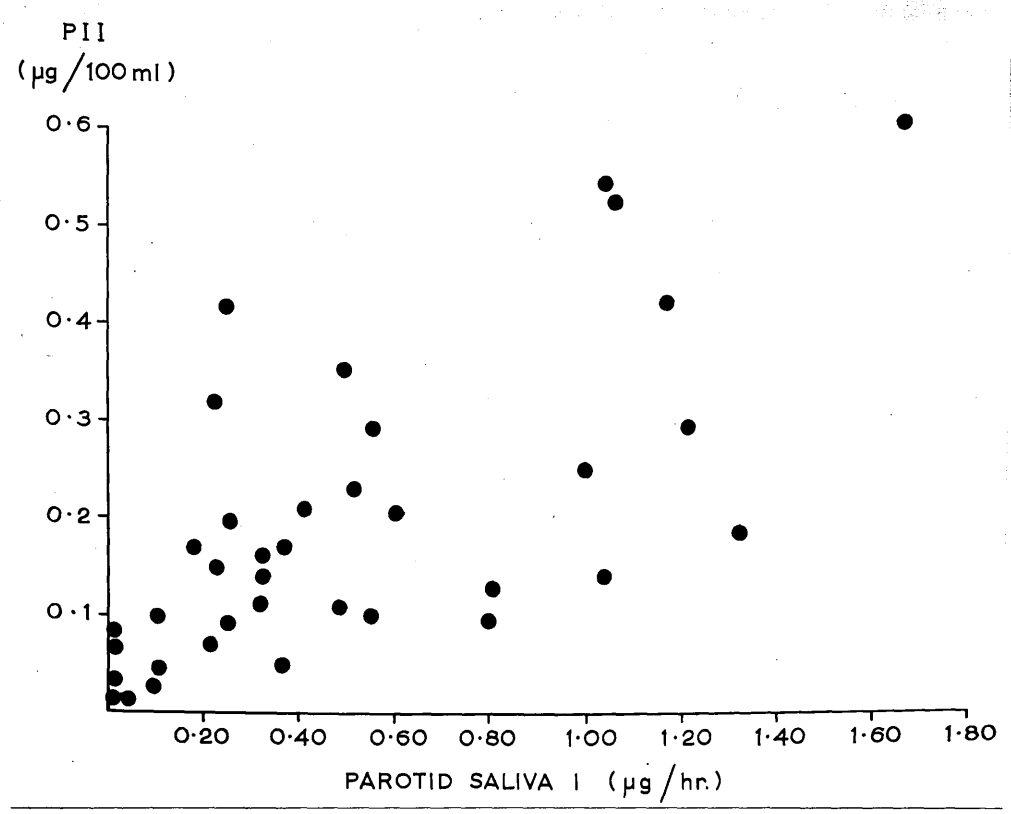
FIGURE III, 10



PAROTID SALIVARY IODIDE CLEARANCE AND PLASMA INORGANIC IODINE (PII) IN THIRTY-EIGHT SUBJECTS.

($r = -0.046$, $0.8 > P > 0.7$)

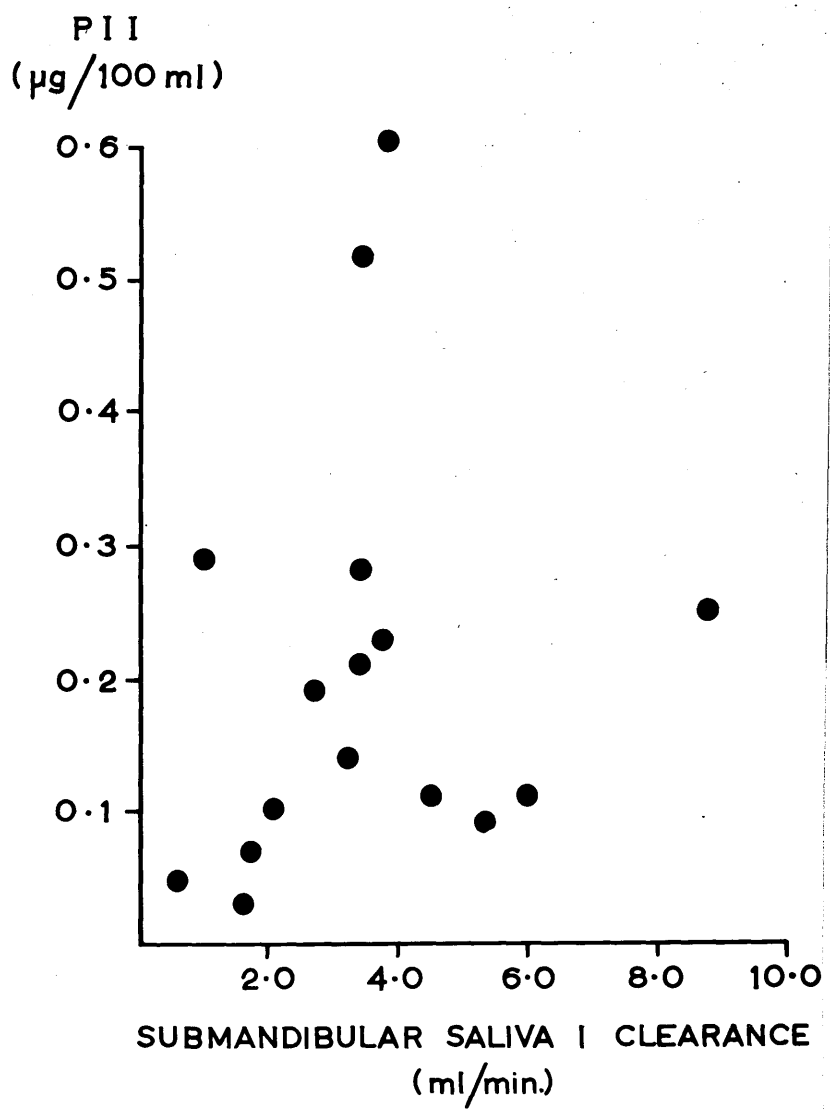
FIGURE III, 11



PAROTID SALIVARY (µg/hr) AND PLASMA INORGANIC IODINE (PII) IN THIRTY-EIGHT SUBJECTS.

Regression equation $y = 0.53x - 0.05$, $r = 0.66$, $P < 0.001$.

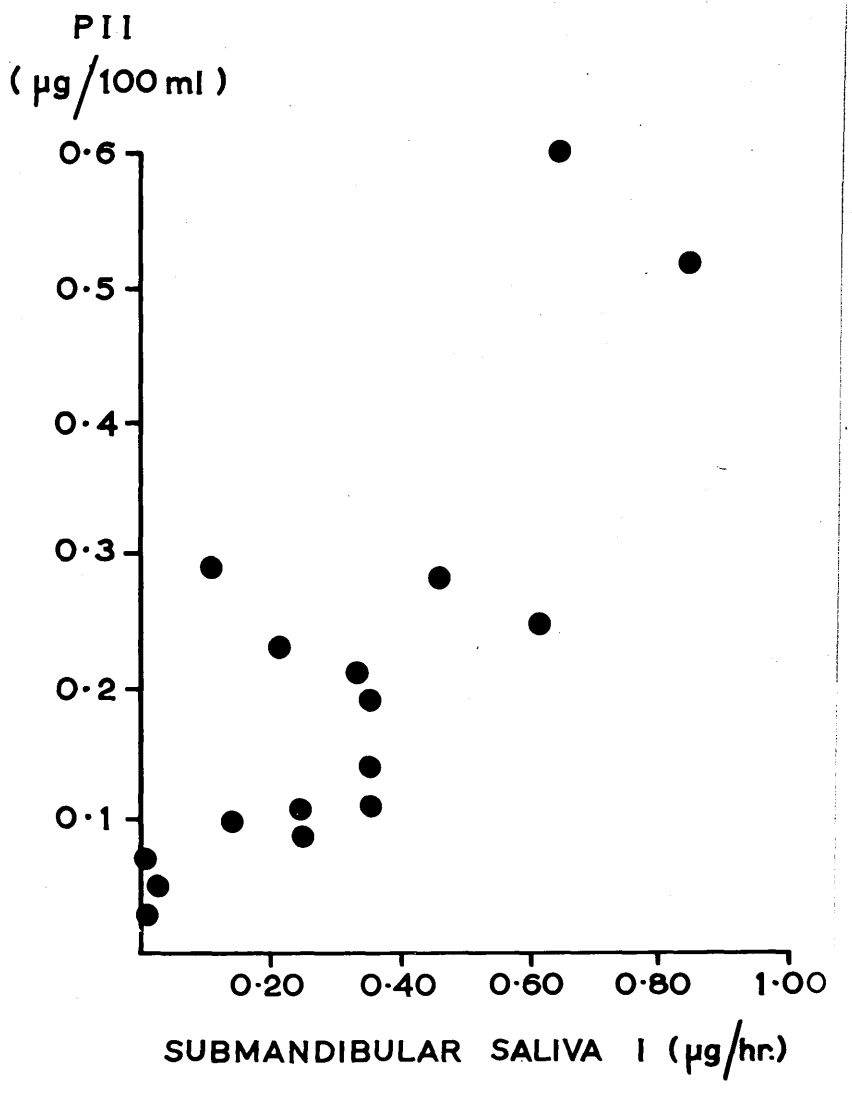
FIGURE III , 12



SUBMANDIBULAR SALIVARY IODIDE CLEARANCE AND PLASMA INORGANIC IODINE (PII) IN SIXTEEN SUBJECTS.

($r = 0.16$, $0.9 > P > 0.8$).

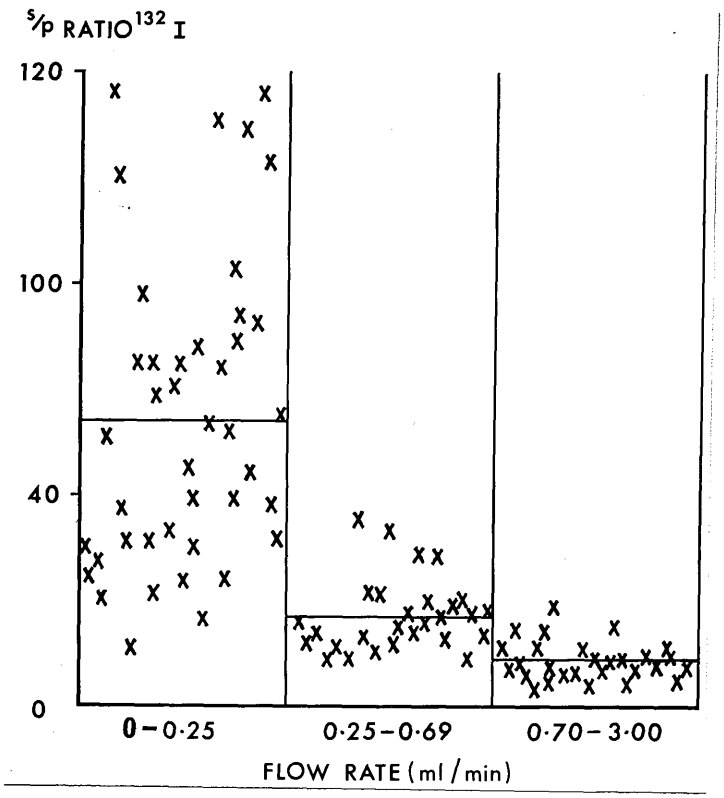
FIGURE III , 13



SUBMANDIBULAR SALIVARY IODINE (µg/hr) AND PLASMA INORGANIC IODINE (PII) IN SIXTEEN SUBJECTS.

Regression equation $y = 0.83x - 0.06$, $r = 0.80$, $P < 0.001$.

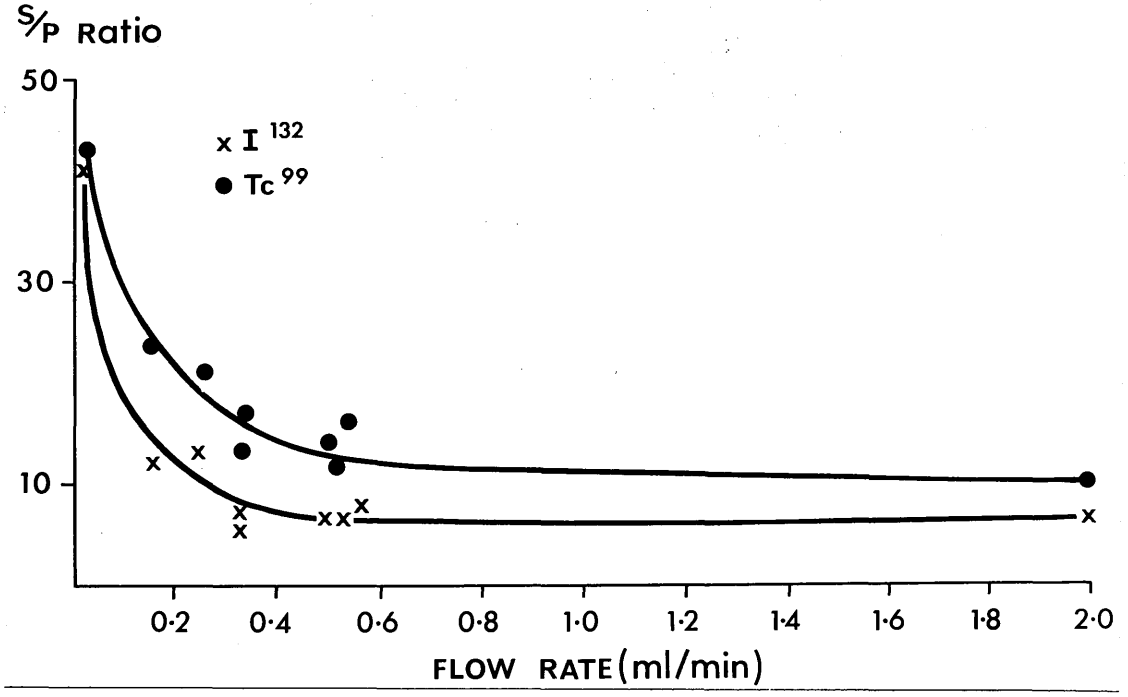
FIGURE III , 14



SALIVA/PLASMA ^{132}I RATIOS IN 58 NORMAL SUBJECTS ARRANGED ACCORDING TO FLOW RATE (ml/min).

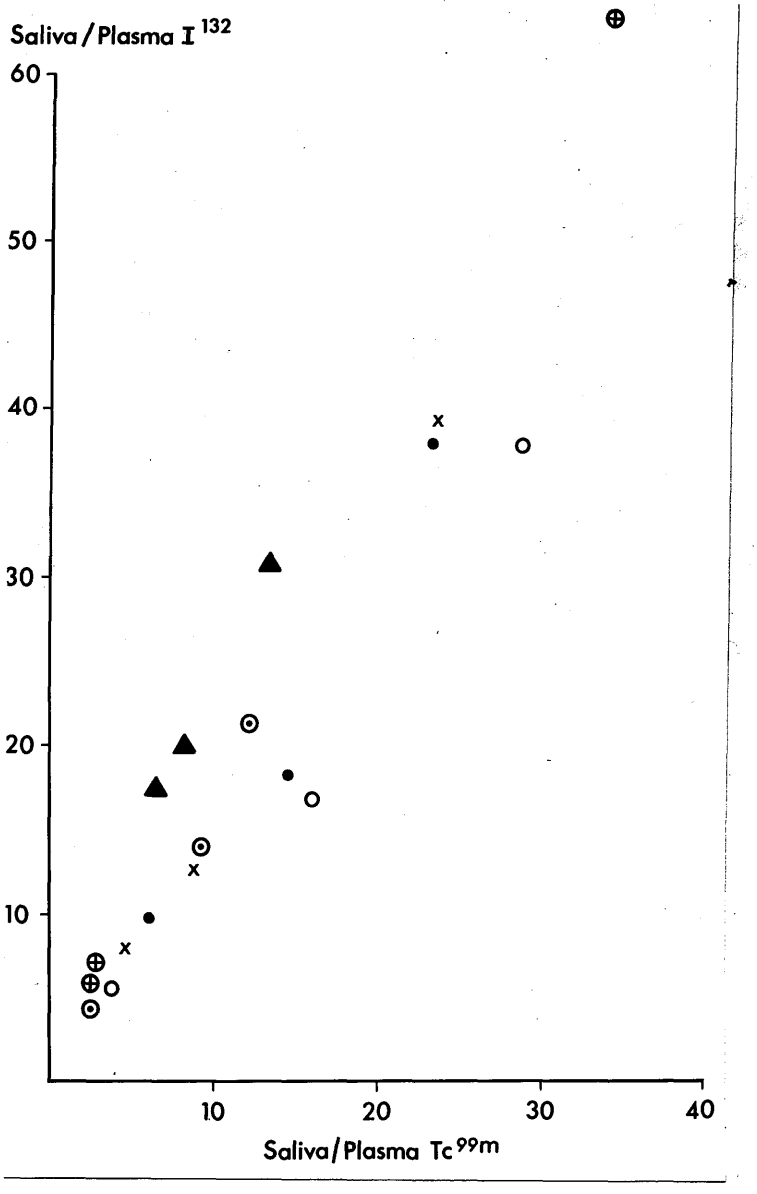
In 37 subjects saliva was collected under 'resting' conditions only and in 21 subjects saliva was collected under 'resting' conditions and after fruit gum and lemon juice stimulation.

FIGURE III , 15



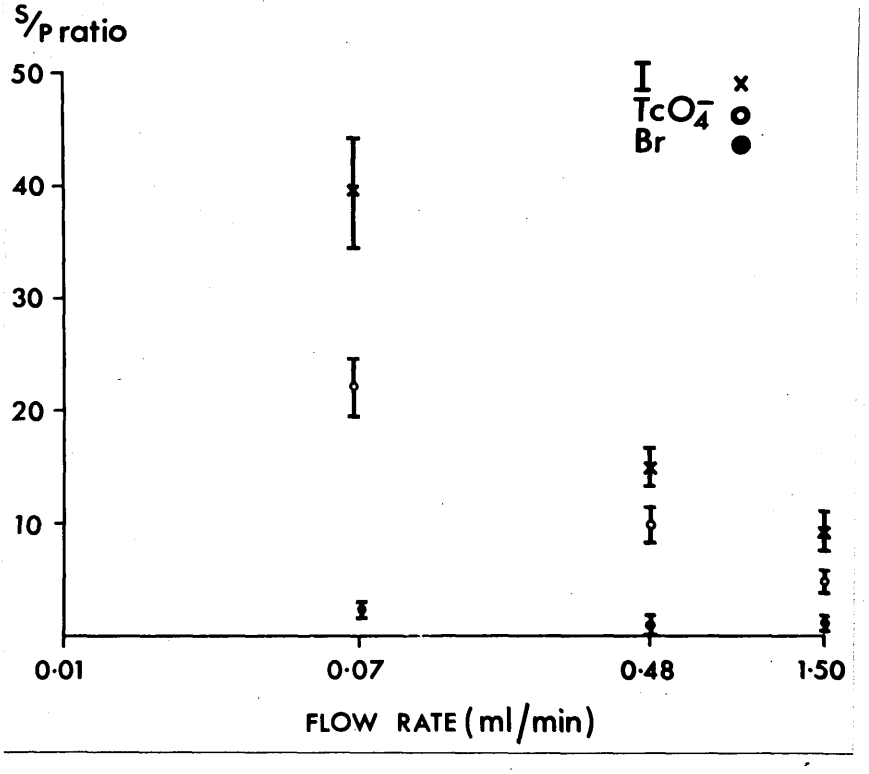
SALIVA/PLASMA RATIOS OF ^{132}I AND ^{99m}Tc AT VARYING FLOW RATES IN ONE SUBJECT.

FIGURE III, 16



RELATION BETWEEN PAROTID SALIVA/PLASMA RATIOS FOR ^{132}I, $^{99m}TcO_4$ IN 6 NORMAL SUBJECTS

FIGURE III, 17



PAROTID SALIVA/PLASMA RATIOS FOR ^{132}I, ^{82}Br, $^{99m}TcO_4$ AT DIFFERENT SALIVARY FLOW RATES.

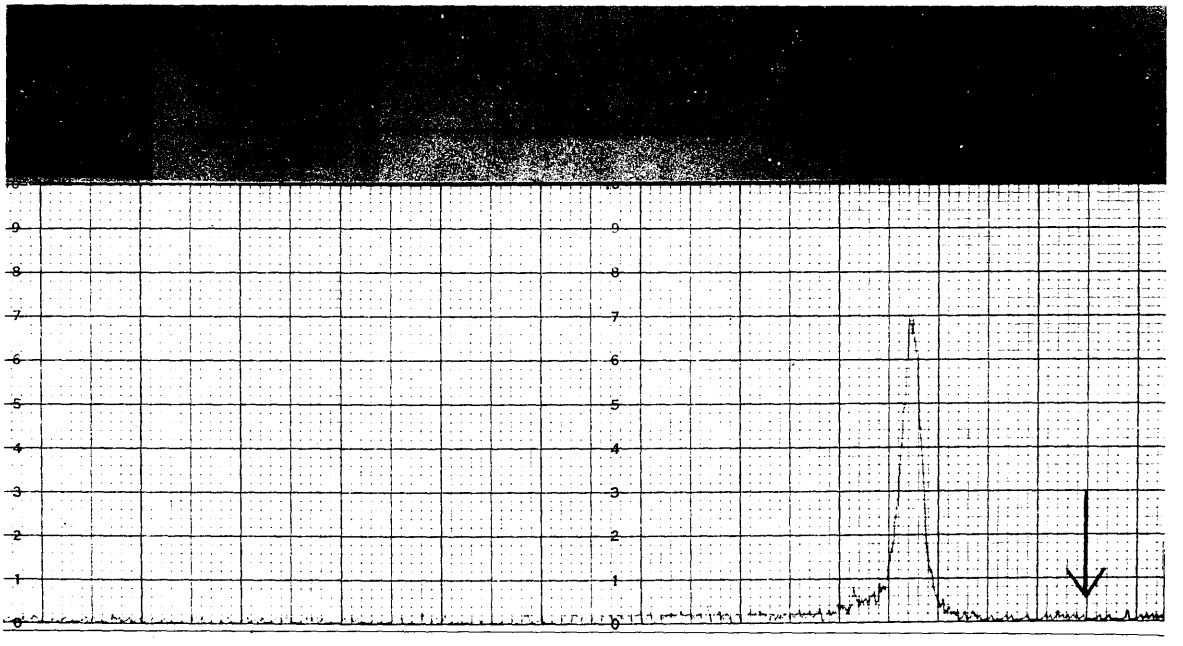
The Mean ± S.E.M. is shown.

TABLE III , 5

PERCENTAGE OF TOTAL SALIVA RADIOACTIVITY AFTER AMBERLITE RESIN AND TCA PRECIPITATION

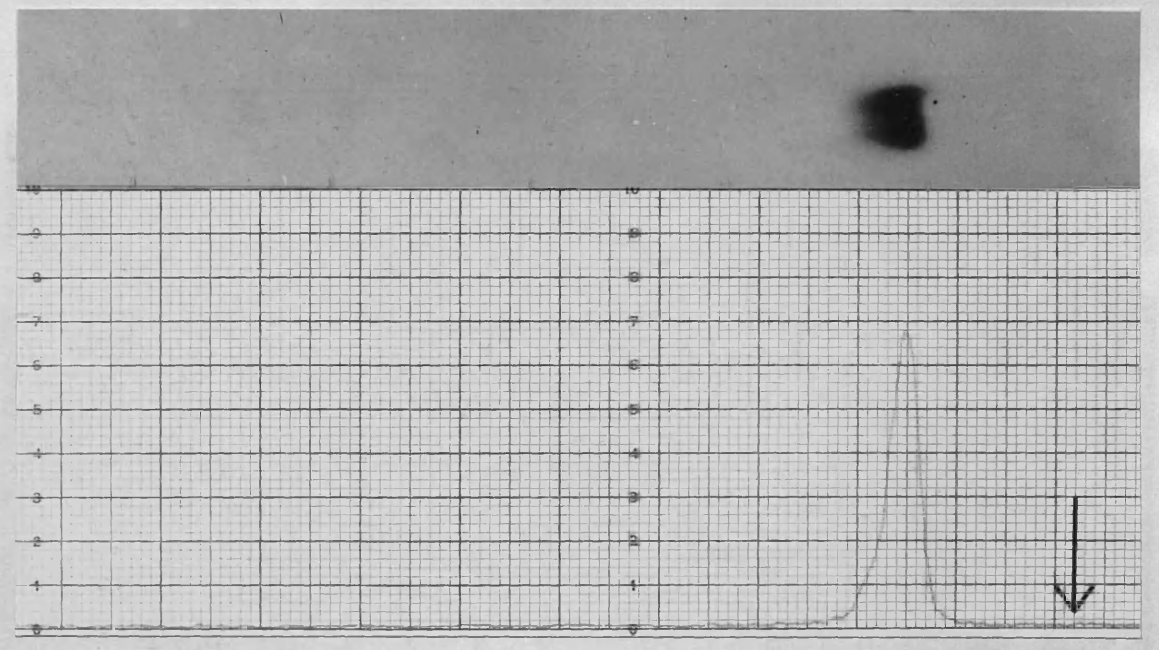
	SALIVA					
	Mixed		Parotid		Submandibular	
	Amberlite resin	TCA ppt	Amberlite resin	TCA ppt	Amberlite resin	TCA ppt
No. of patients	11	11	18	9	5	1
Range	0.1-4.8%	0.4-24.7%	0.00-0.5%	1.7-23.2%	0.0-0.5%	5.4%
Mean	1.5%	10.2%	0.3%	7.8%	0.2%	-
S.E. of Mean	0.46%	2.68%	0.10%	2.47%	0.92%	-

FIGURE III , 18



RADIOCHROMATOGRAM OF PAROTID SALIVA FROM A THYROTOXIC PATIENT. ONLY IODIDE IS DEMONSTRATED.

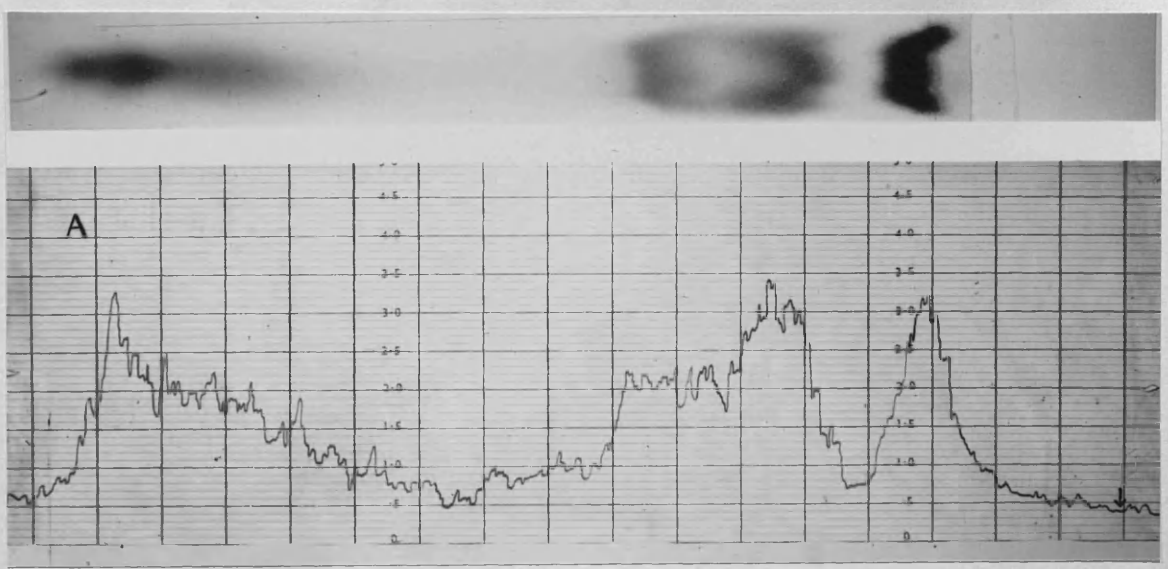
FIGURE III, 19



RADIOCHROMATOGRAM OF MIXED SALIVA. ONLY IODIDE IS DEMONSTRATED.

The origin is designated by the arrow on the right of the chromatogram.

FIGURE III , 20



RADIOCHROMATOGRAM OF STANDARDS.

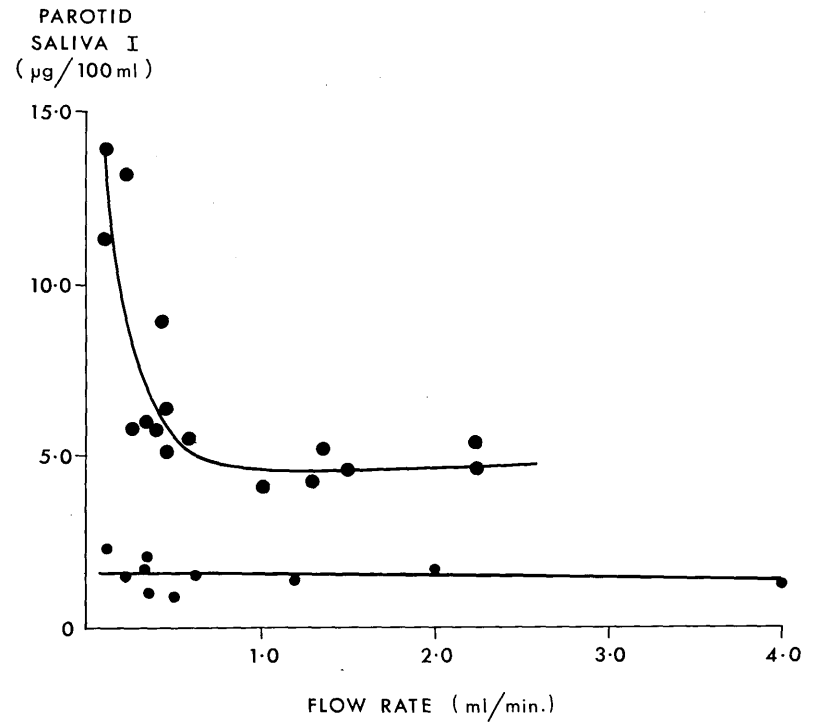
From right to left the main bands are I^-, MIT, DIT, T_3 and T_4.

TABLE III, 6

PERCENTAGE OF TOTAL SALIVA RADIOACTIVITY
AFTER AMBERLITE RESIN IN TWO PATIENTS
FOUR DAYS FOLLOWING 100mc ^{131}I.

PATIENT	THYROID STATUS	MIXED	PAROTID
1	Thyrotoxic	6.64	0.87
2	Euthyroid	1.77	1.49

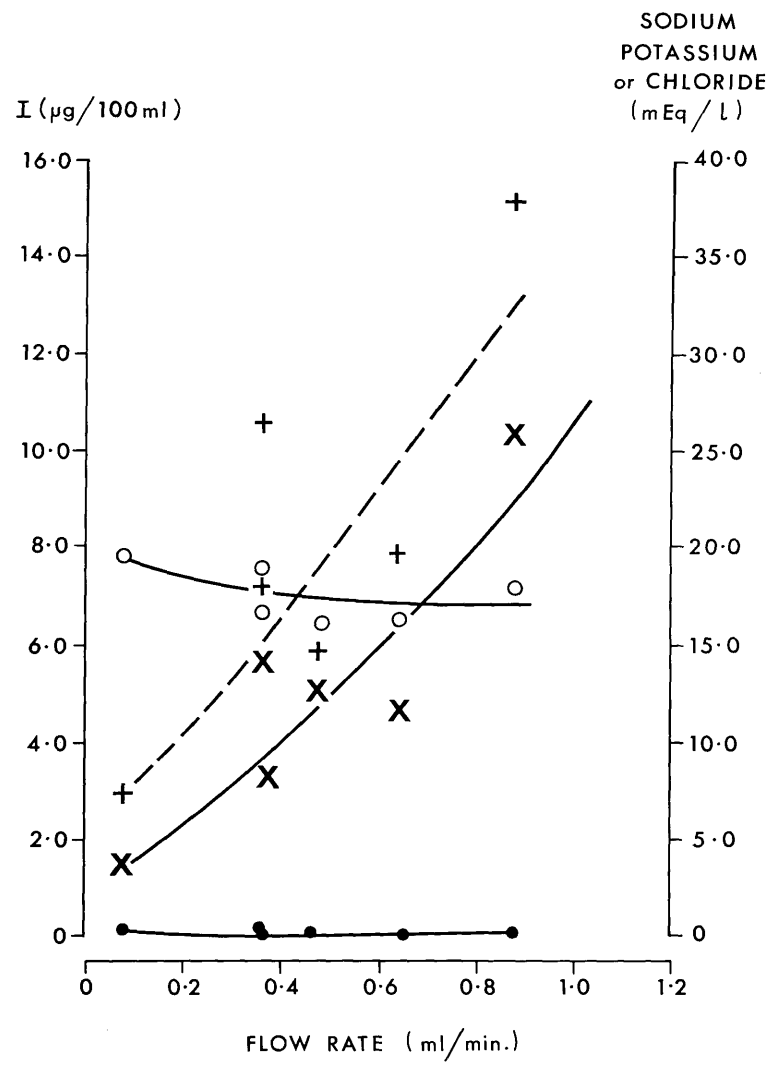
FIGURE III , 21



PAROTID SALIVARY IODIDE CONCENTRATIONS BEFORE AND AFTER POTASSIUM PERCHLORATE

Parotid salivary iodide concentration at different flow rates in one subject. The upper line represents values before potassium perchlorate and the lower line values after potassium perchlorate.

FIGURE III, 22

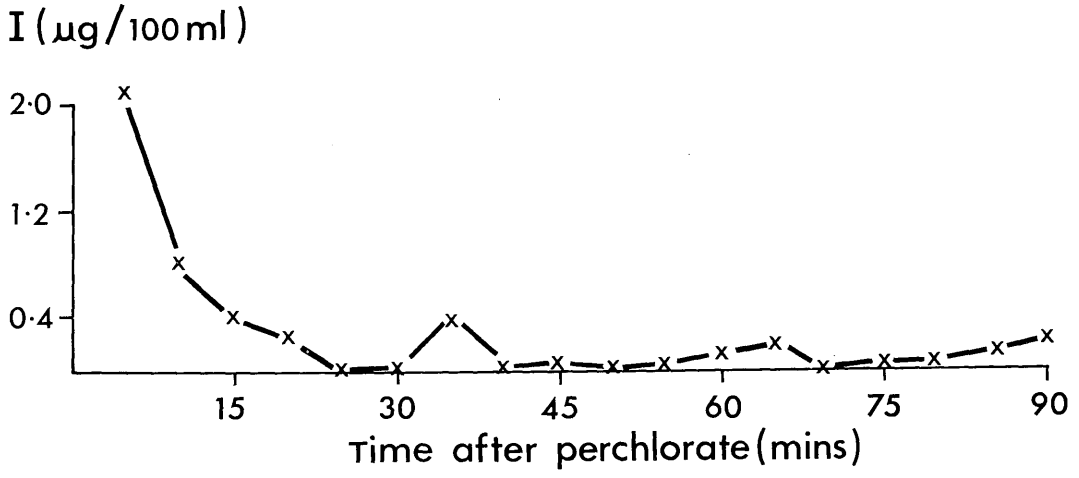


VARIATIONS WITH FLOW RATE IN IODIDE, SODIUM, POTASSIUM AND CHLORIDE CONCENTRATION IN SUBMANDIBULAR SALIVA AFTER POTASSIUM PERCHLORATE

●——● iodide x——x sodium

0——0 potassium +——+ chloride

FIGURE III , 23



THE EFFECT ON PAROTID SALIVARY IODIDE SECRETION DURING 90 MINUTES AFTER THE ORAL ADMINISTRATION OF 500 mg POTASSIUM PERCHLORATE.

TABLE III, 8

SALIVA/PLASMA RATIOS OF ^{132}I, ^{99m}Tc, ^{82}Br, BEFORE AND 30 MINUTES AFTER POTASSIUM PERCHLORATE (500 mg orally).

Parotid saliva of 1 normal subject at three flow rates - 'resting', after fruit gum and lemon juice stimulation.

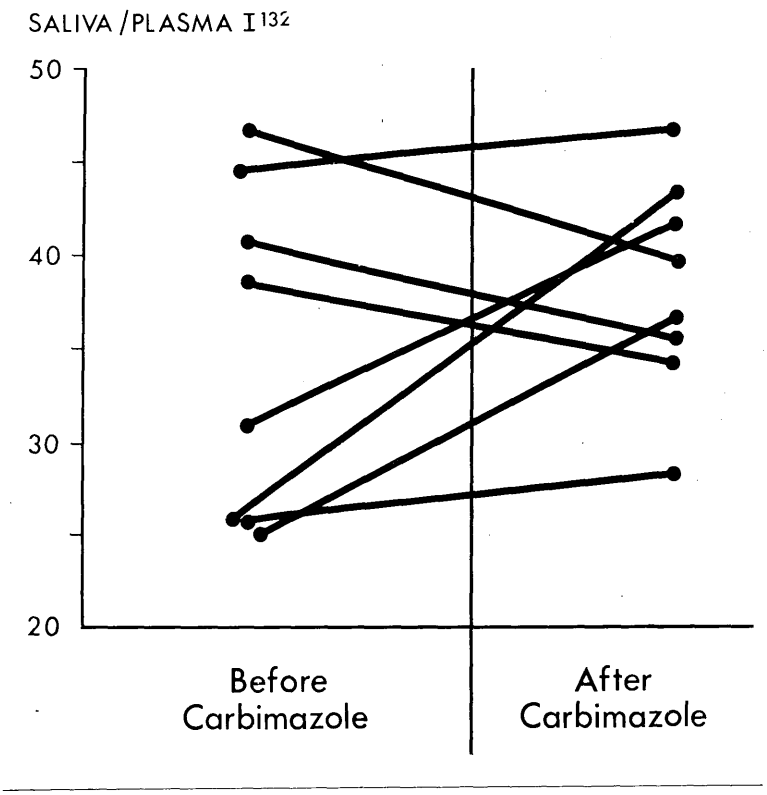
	'Resting'	Fruit Gum	Lemon Juice
Before Perchlorate			
Flow rate (Vol/min.)	.04	.35	.89
Saliva/plasma ^{132}I	66.30	15.40	14.80
" " $^{99m}TcO_4$	39.50	11.56	7.77
" " ^{82}Br	1.65	0.59	0.79
After Perchlorate			
Flow rate (Vol/min.)	.06	.37	.77
Saliva/plasma ^{132}I	10.00	3.20	1.90
" " $^{99m}TcO_4$	3.79	0.83	0.68
" " ^{82}Br	0.17	0.08	0.29

TABLE III , 9

SALIVA/PLASMA RATIOS OF ^{132}I, ^{99m}Tc, ^{82}Br, BEFORE AND 30 MINUTES AFTER 500 mg POTASSIUM PERCHLORATE ORALLY IN SUBMANDIBULAR SALIVA OF ONE NORMAL SUBJECT AT THREE FLOW RATES - 'RESTING', AFTER FRUIT GUM AND LEMON JUICE STIMULATION

	'Resting'	Fruit Gum	Lemon Juice
Before Perchlorate			
Saliva/plasma ^{132}I	23.00	10.32	7.30
" " ^{99m}Tc	9.45	5.20	3.50
" " ^{82}Br	1.09	1.03	1.12
After Perchlorate			
Saliva/plasma ^{132}I	8.90	3.00	1.83
" " ^{99m}Tc	1.86	0.65	0.45
" " ^{82}Br	0.26	0.20	0.58

FIGURE III, 24



SALIVA/PLASMA ^{132}I BEFORE AND AFTER CARBIMAZOLE

Saliva/plasma ^{132}I ratio in 8 subjects before and after 2 weeks carbimazole 30 mgs/day.

TABLE III , 10

RESULTS OF ABSOLUTE IODINE UPTAKE BY THYROID GLAND AND SECRETION OF IODINE IN PAROTID SALIVA

	Euthyroid (21 patients)			Hyperthyroid (24 patients)			Hypothyroid (12 patients)		
	Mean	SEM*	Range	Mean	SEM	Range	Mean	SEM	Range
PBI(ug/100ml)	5.7	0.22	3.9 - 7.5	12.4	0.53	8.1 - 19.1	1.7	0.30	0.8 - 3.6
Plasma inorganic iodine (µg/100 ml)	0.19	0.040	0.05 - 0.82	0.09	0.015	0.01 - 0.29	0.25	0.052	0.08 - 0.57
Thyroid absolute iodine uptake (µg/hr)	2.1	0.36	0.4 - 5.9	19.6	2.68	5.9 - 43.9	1.0	0.21	0.1 - 2.3
Parotid saliva volume (ml/30 min)	4.8	0.77	0.9 -14.0	4.1	0.68	0.5 - 16.8	3.8	0.70	1.0 - 8.7
Parotid saliva iodine (µg/hr)	0.62	0.115	0.01 - 2.05	0.31	0.071	0.04 - 1.75	0.61	0.103	0.11 - 1.12

* Standard error of the mean.

TABLE III , 11

RESULTS OF ABSOLUTE IODINE UPTAKE BY THE SUBMANDIBULAR GLAND

	Euthyroid (8 patients)			Hyperthyroid (16 patients)			Hypothyroid (9 patients)		
	Mean	SEM *	Range	Mean	SEM	Range	Mean	SEM	Range
Plasma inorganic iodine (µg/100ml)	0.14	0.02	0.05- 0.24	0.10	0.02	0.01- 0.29	0.15	0.04	0.08- 0.41
Submandibular saliva vol. (ml/30 min)	3.7	1.15	1.0 - 11.2	5.5	0.97	1.5 -16.5	4.7	1.39	0.8 -15.0
Submandibular saliva iodine (µg/hr.)	0.27	0.051	0.01- 0.46	0.28	0.064	0.02- 0.94	0.47	0.146	0.05- 1.18

* Standard error of the mean

TABLE III , 12

CLINICAL DETAILS OF THE 15 PATIENTS STUDIED - GENERAL

PATIENT	AGE	SEX	KERATO CONJUNCT-IVITIS SICCA	XERO STOMIA	RHEUMATOID ARTHRITIS	SALIVARY GLAND ENLARGE-MENT	ASSOC-IATED DISEASE
1	62	M	+	+	-	-	-
2	63	F	+	+	+	-	-
3	54	M	+	+	+	-	Goitre
4	66	F	+	+	-	-	-
5	56	F	+	+	+	-	Myxoedema Myasthenia Gravis
6	53	F	+	+	-	-	Anaemia
7	78	F	+	+	+	+	-
8	54	F	+	+	+	-	-
9	73	F	+	+	-	-	Raynaud's disease
10	53	F	+	+	-	-	Thyrotoxi-cosis Raynaud's disease
11	63	F	+	+	-	-	-
12	59	M	+	+	-	-	-
13	54	F	+	+	-	+	-
14	64	F	+	+	-	-	-
15	59	F	+	+	+	-	-

TABLE III, 13

LABORATORY DETAILS IN THE 15 PATIENTS STUDIED

PATIENT	W.B.C. (/cmm.)	E.S.R. (mm. in 1st hr.)	H.b. (g/100ml)	Globulins (g/100ml)	S.S.C.A. Test [1]	Hyland R.A. Test	L.E. Test Cells	L.E. Test Latex	A.N.F. Test [2]	Non-organ specific Prec. Test [3]	T.T.R.C. Test [4]
1	5,000	32	14.1	3.6	+ve (128)	+ve	-ve	-ve	+ve (1000H)	-ve	+ve (4000)
2	5,200	70	13.3	2.6	+ve (256)	+ve	-ve	-ve	+ve (100H)	-ve	-ve
3	5,200	40	15.4	3.8	-ve	+ve	-ve	-ve	+ve	-ve	-ve
4	3,900	38	12.6	4.2	-ve	+ve	-ve	-ve	-	-	-ve
5	3,400	20	13.3	4.3	+ve (128)	+ve	-ve	-ve	+ve (1000S)	+ve	+ve (4000)
6	9,700	80	8.0	2.1	-ve	-ve	-ve	-ve	+ve (16H)	-ve	-ve
7	6,000	15	11.8	2.2	+ve (64)	+ve	-ve	-ve	+ve (16S)	-ve	+ve (4000)
8	6,100	8	10.3	3.3	-ve	+ve	-ve	-ve	+ve (16H)	+ve	-ve
9	6,300	16	13.0	2.0	+ve (64)	+ve	+ve	-ve	+ve (64H)	-ve	-ve
10	9,700	10	15.7	-	-ve	+ve	-ve	-ve	-ve	-ve	-ve
11	3,300	25	12.7	2.9	-ve	+ve	-ve	-ve	-ve	-ve	-ve
12	12,600	41	16.1	3.8	-ve	+ve	-ve	-ve	-ve	-ve	-ve
13	4,500	10	15.0	3.5	-ve	+ve	-ve	-ve	-ve	-ve	+ve (256)
14	7,200	20	13.2	3.4	-ve	-ve	-ve	-ve	-ve	-ve	-ve
15	5,650	21	13.3	3.0	+ve (128)	+ve	-ve	-ve	+ve (16H)	-ve	-ve

1. SSCA = sensitized sheep cell agglutination test for rheumatoid factor, starting titre 1:32 or greater. 2. ANF = antinuclear factor. H = homogenous staining. S = speckled staining, starting titre 1:16 or greater. 3. Precipitating auto-antibodies to tissue components, undiluted sera. 4. TRC Test = thyroglobulin tanned red cell test, starting titre 1:16 or greater.

TABLE III. 14

SIALOGRAPHIC FINDINGS, FLOW RATE MEASUREMENTS AND SALIVA/PLASMA ^{132}I RATIOS IN THE 15 PATIENTS STUDIED

	SIALOGRAPHY					FLOW RATE PAROTID SALIVA (ml/min.)				SALIVA/PLASMA ^{132}I RATIO			
Patient	Normal	Atrophy	Punctate	Globular	Cavitary	Resting	Wax	Fruit Gum	Lemon Juice	Resting	Wax	Fruit Gum	Lemon Juice
1	0	X	0	X	0	0	-	0.09	0.38	-	-	11.6	8.0 †
2	0	X	0	0	0	0	0.11 *	-	-	-	7.2 * †	-	-
3	0	X	X	0	0	0	-	0.04	0.10	-	-	51.3	52.1
4	0	X	0	0	X	0	0.004	0.03	0.08	-	22.1	11.0	5.6 †
5	0	X	X	0	0	0.04	-	0.11	0.22	24.2	-	16.0	9.2 †
6	0	0	X	0	0	0.001	-	0.14	0.40	-	-	60.9	27.4
7	0	X	0	0	X	0	0	0	0	-	-	-	-
8	0	X	0	X	0	0	0	0	0	-	-	-	-
9	0	X	0	0	X	0	0	0	0	-	-	-	-
10	X	0	0	0	0	0	-	0.19	0.68	-		37.9	14.8
11	0	0	X	0	0	0	0.06	0.28	0.70	-	23.7	-	9.7
12	X	0	0	0	0	0.04	-	0.48	2.10	59.8	-	21.4	10.7
13	X	0	0	0	0	0.05	-	0.30	1.30	24.8	-	20.7	14.5
14	X	0	0	0	0	0.14	-	0.53	1.50	106.3	-	48.8	31.8
15	X	0	0	0	0	0.08	-	0.41	0.78	73.5	-	18.5	15.3

* Mixed saliva only obtained

† Below normal range at this flow rate (Table III. 5)

TABLE III , 15

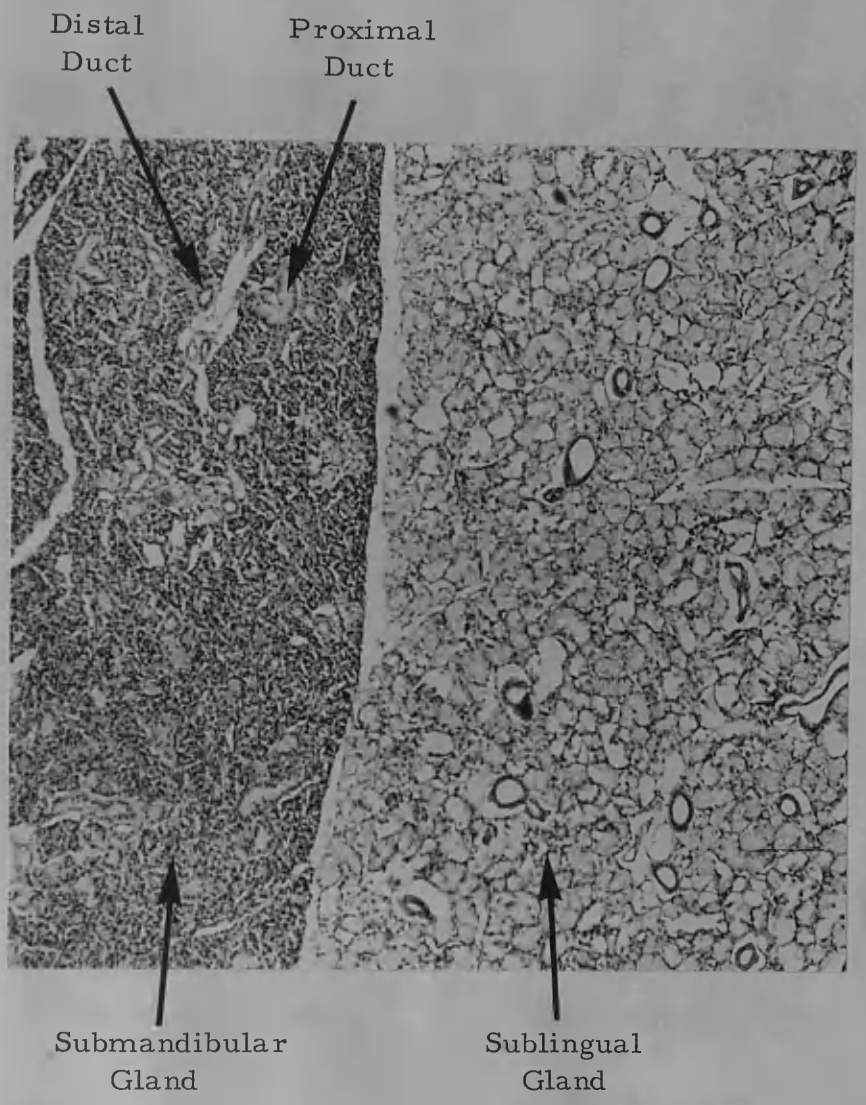
PAROTID SALIVARY AND PLASMA IODIDE CONCENTRATIONS FOLLOWING A TRACER DOSE ^{132}I (25 μc) IN NINE PATIENTS WITH FIBROCYSTIC DISEASE.

Saliva was collected during fruit gum stimulation.

	Subject	Age (yrs)	Flow Rate (ml/min)	Salivary Iodide (ug/100 ml)	P.I.I. (ug/100 ml)	Saliva/Plasma ^{132}I
	1	5	0.27	4.1	0.20	20.0
	2	12	0.39	2.9	0.15	20.0
	3	10	0.35	2.5	0.13	19.3
	4	9	0.45	1.1	0.07	14.5
	5	11	0.29	4.1	0.16	25.5
	6	6	0.24	1.9	0.13	14.5
	7	7	0.20	4.6	0.15	30.8
	8	7	0.53	4.7	0.30	15.3
*	9A	11	0.25	72.0	2.31	53.7
	9B	11	0.24	3.9	0.26	14.8

9B are results of patient 9A three weeks after stopping cough mixture.

FIGURE III, 25

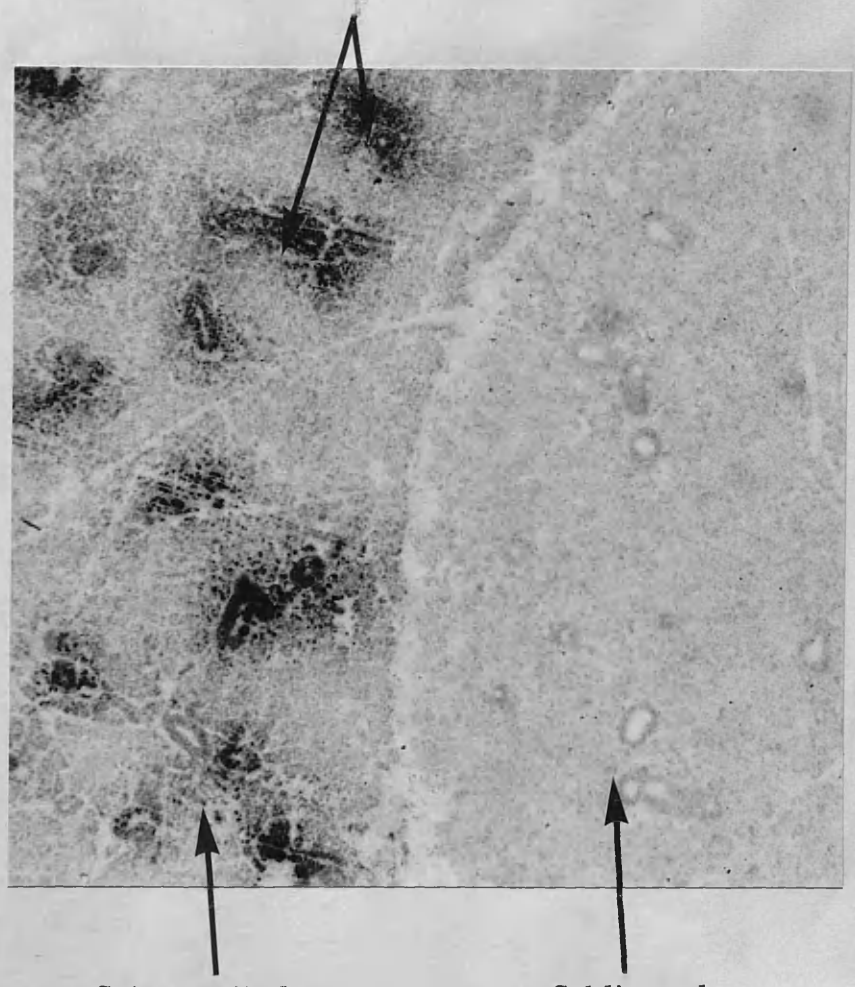


ADULT MALE HAMSTER. PHOTOMICROGRAPH SHOWING SUBMANDIBULAR GLAND TISSUE (LEFT) AND SUBLINGUAL GLAND (RIGHT.)

Stained H & E.

Magnification x 75

FIGURE III , 26



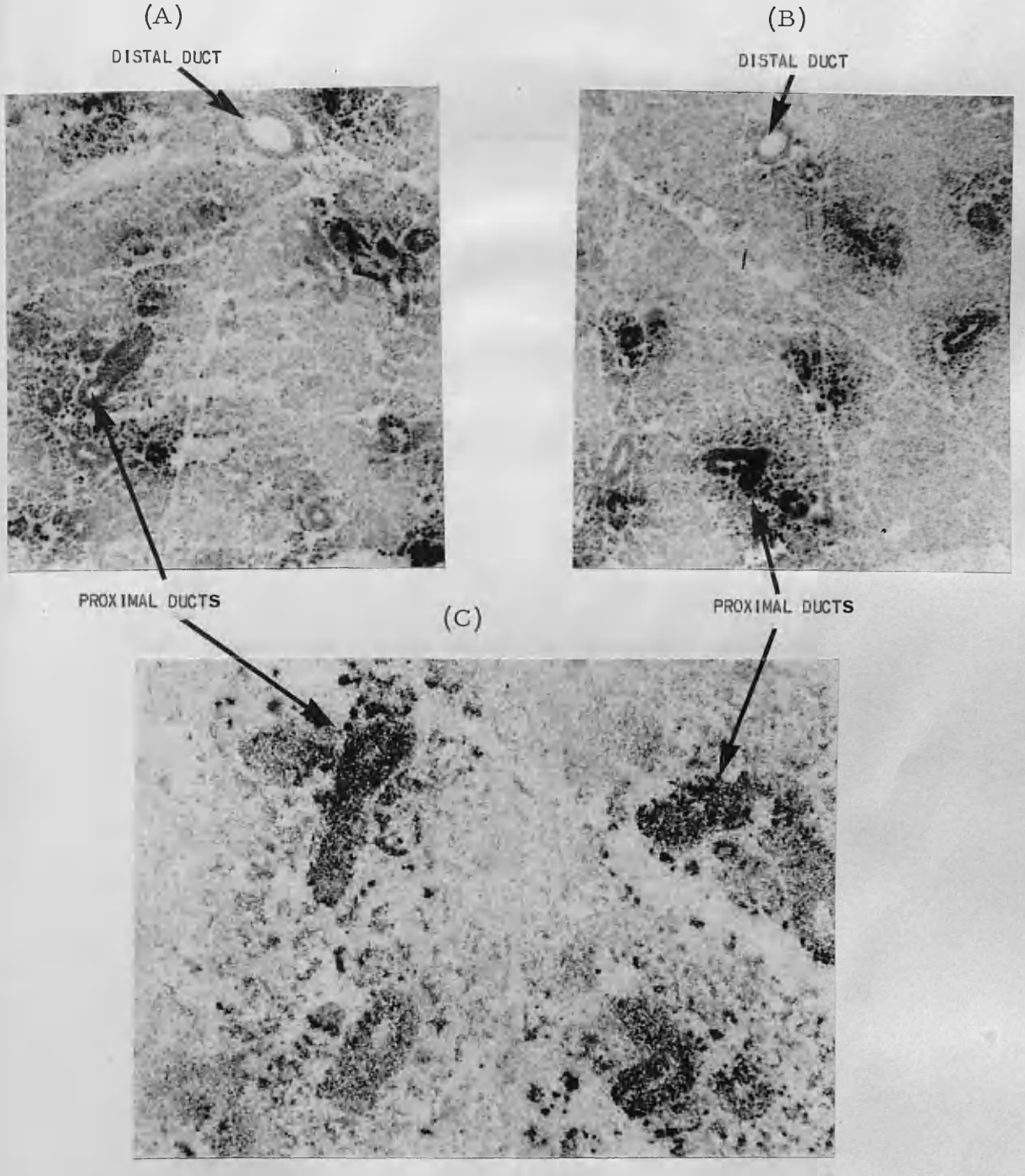
ADULT MALE HAMSTER - AUTORADIOGRAPH OF SUBMANDIBULAR GLAND (Left) AND SUBLINGUAL GLAND (Right) AS IN PREVIOUS FIGURE III , 25

In the submandibular gland concentration of ^{131}I is shown over the proximal ducts and a less intense image is present over the acini. Comparatively little radioactivity is seen over the sublingual gland tissues.

Stain Neutral Red

Magnification x 75

FIGURE III, 27



AUTORADIOGRAPHS OF HAMSTER SUBMANDIBULAR GLAND

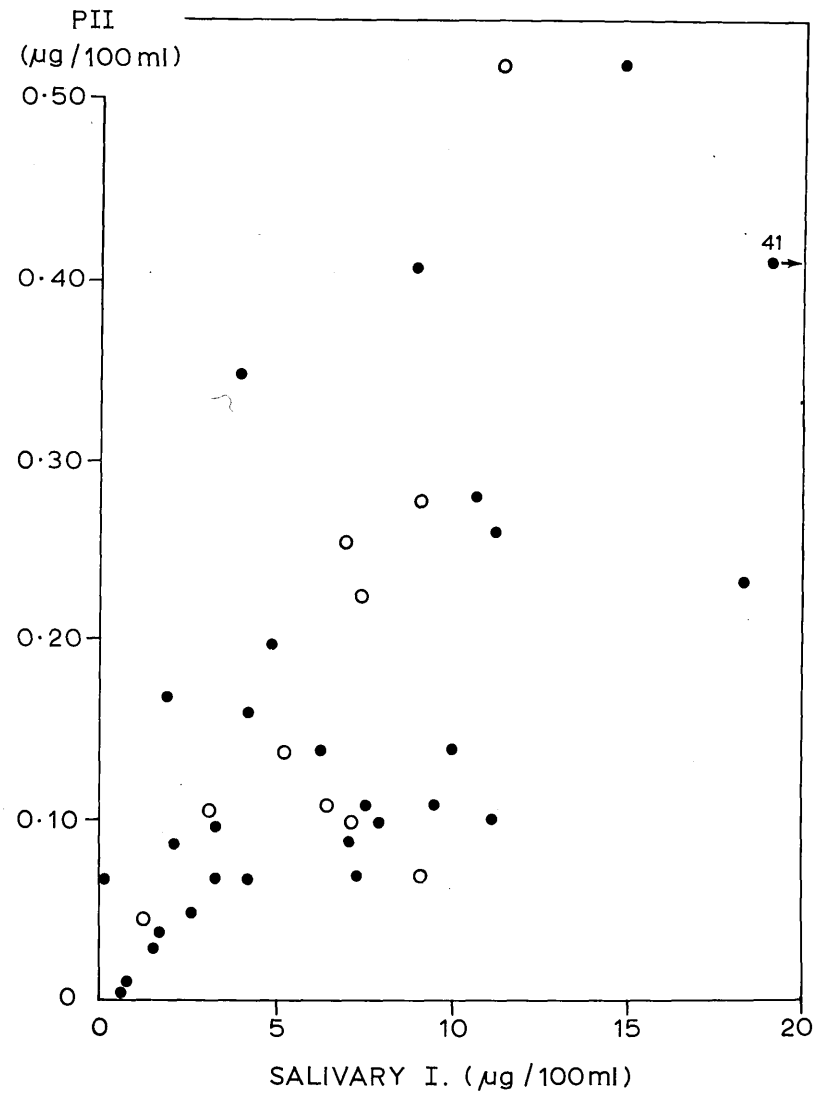
showing - intense concentration of ^{131}I around proximal ducts

- slight " " ^{131}I over acini and distal ducts

Stain neutral red

Magnification A & B x 75 C x 200

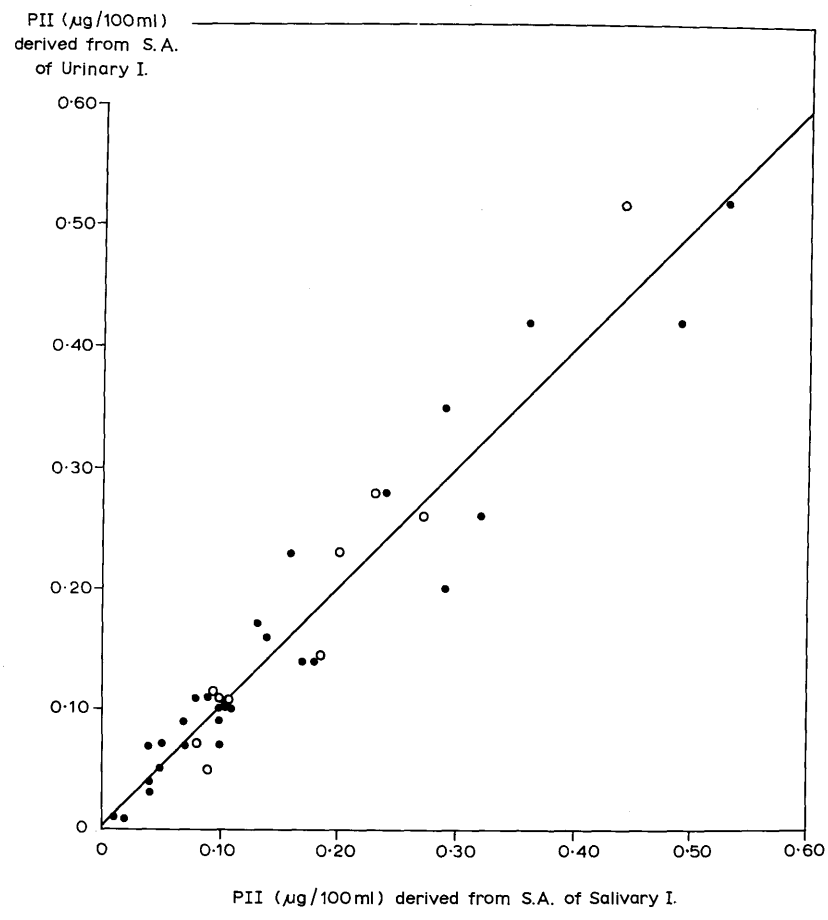
FIGURE III, 28



RELATIONSHIP BETWEEN PII AS DERIVED FROM THE SALIVARY I^{127} AND THE SPECIFIC ACTIVITY OF URINARY IODINE IN 28 EUTHYROID PATIENTS.

●, parotid saliva; O, submandibular saliva
regression equation is Y = 0.982 + 0.0112 X
correlation coefficient r = 0.61, P<0.001.

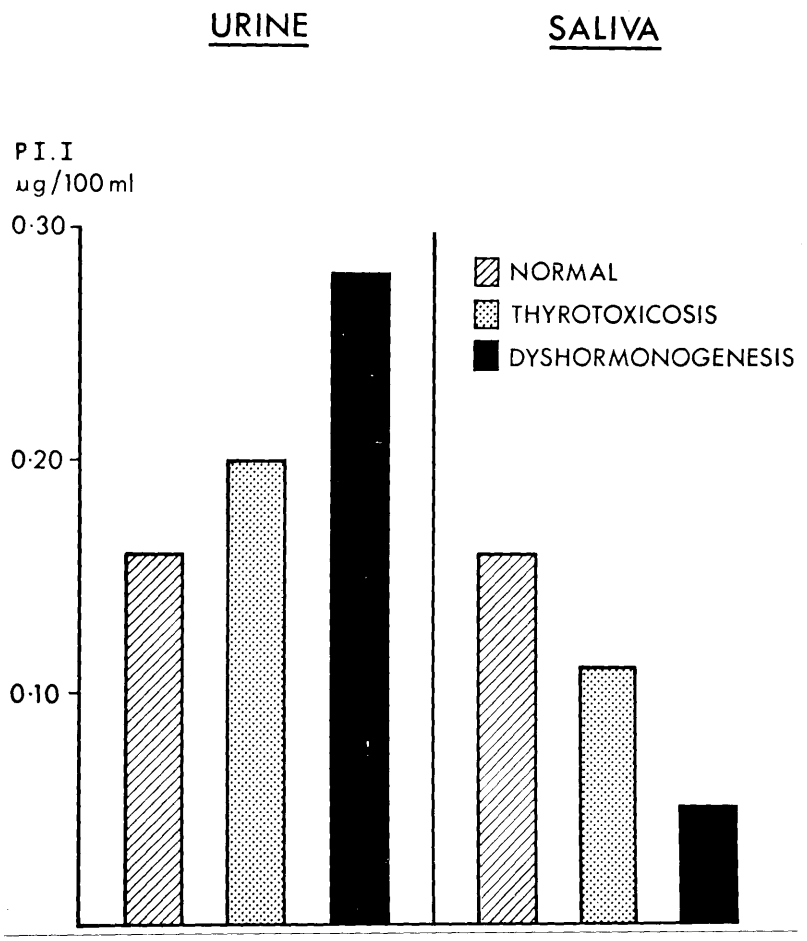
FIGURE III, 29



RELATIONSHIP BETWEEN PII AS DERIVED FROM THE SPECIFIC ACTIVITY OF URINARY IODINE AND SPECIFIC ACTIVITY OF SALIVARY IODINE IN 28 EUTHYROID PATIENTS.

● , parotid saliva O, submandibular saliva regression equation is $Y = 0.03 + 0.985\ X$, correlation coefficient $r = 0.96$, $P < 0.001$.

FIGURE III , 30



COMPARISON OF PII VALUES IN NORMAL SUBJECTS, PATIENTS WITH THYROTOXICOSIS AND ONE PATIENT WITH DEHALOGENASE DEFICIENCY.

On the left the falsely raised values in thyrotoxicosis and dyshormonogenesis derived from the urine and on the right the true values derived from the specific activity of the saliva after a tracer dose of ^{132}I.

TABLE III, 16

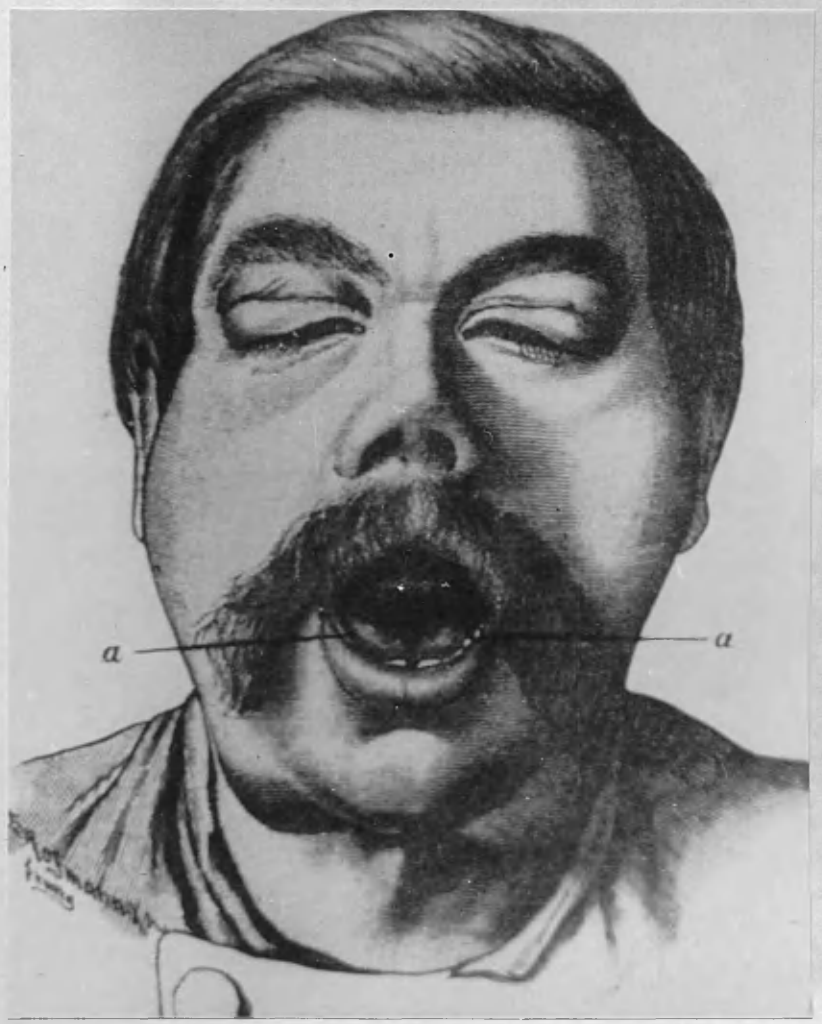
EFFECT OF THYROID STIMULATING HORMONE (TSH) ON SALIVA/PLASMA ^{132}I RATIO.

Parotid Saliva Was Collected After Fruit Gum Stimulation

	$S/_p$ ^{132}I
Control	31.7
After 10 units TSH	28.8
After 20 units TSH	33.2
After 40 units TSH	31.2

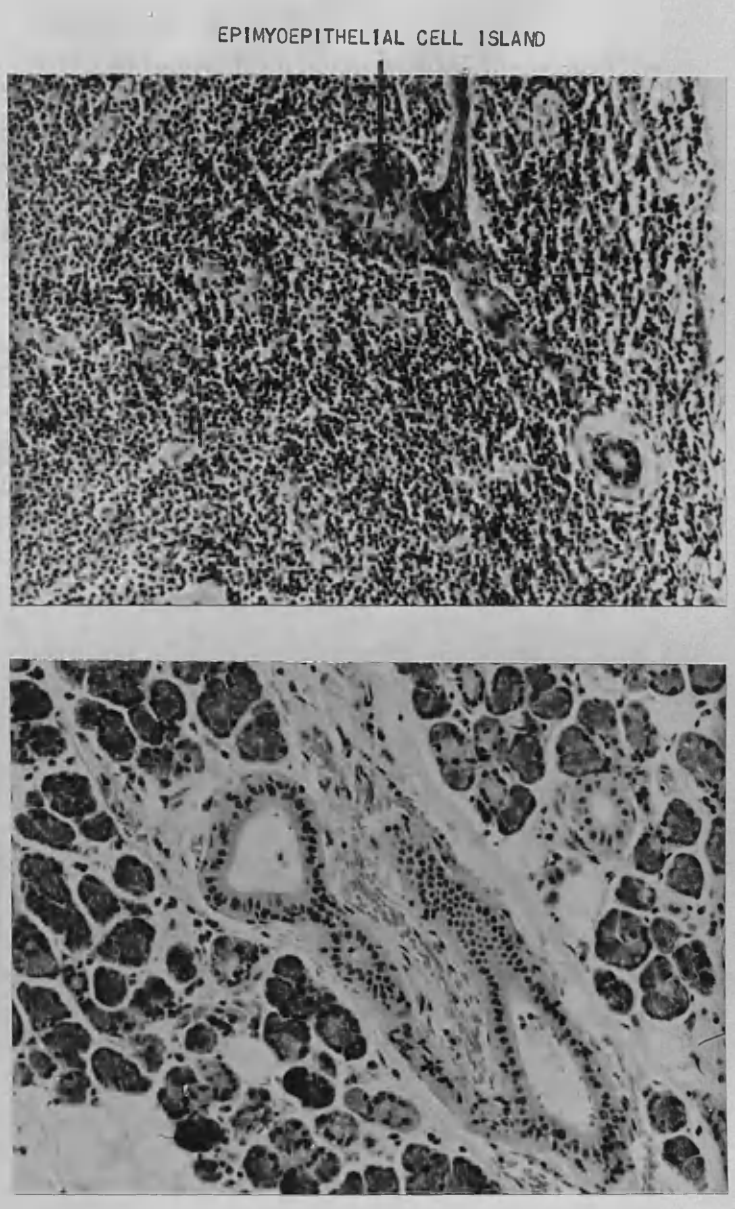
PART IV

FIGURE IV, 1



THE EXTENSIVE BILATERAL ENLARGEMENT OF THE SALIVARY GLANDS IN THE PATIENT ORIGINALLY DESCRIBED BY MIKULICZ.

FIGURE IV, 2



HISTOPATHOLOGICAL CHANGES IN HUMAN SUBMANDIBULAR SALIVARY GLAND IN SJÖGREN'S SYNDROME COMPARED WITH NORMAL GLAND.

(A) SJÖGREN'S SYNDROME showing dense lymphocytic infiltration; acinar atrophy; ductal hyperplasia and epimyoepithelial cell island formation.

(B) NORMAL GLAND

Magnification x 210

TABLE IV, 1

DURATION OF SICCA COMPONENTS AND RHEUMATOID ARTHRITIS IN THE 30 PATIENTS STUDIED.

GROUP A - RHEUMATOID ARTHRITIS + SICCA COMPONENTS.

Patient	A1	A2	A3	A4	A5	A6	A7	A8	A9	A10	A11	A12
Duration of KCS (yrs.)	25	8	3/4	22	11	4	1	8	-	1	1	1
Duration of Xerostomia (yrs.)	25	7	8	22	1/2	6	2	8	16	1	2	1
Duration of Rheumatoid Arthritis (yrs.)	25	10	8	22	11	2	6	8	16	5	14	5

GROUP B - SICCA SYNDROME

Patient	B1	B2	B3	B4	B5	B6	B7	B8	B9	B10	B11	B12	B13	B14	B15	B16	B17	B18
Duration of KCS (yrs.)	12	2	2	4	10	1	5	1	4	8	6	1	1	1	1	3	4	5
Duration of Xerostomia (yrs.)	12	5	1	4	10	1	5	3	2	8	4	2	2	3	1	5	3	5

TABLE IV, 2

CLINICAL DETAILS OF THE 30 PATIENTS STUDIED (A) GENERAL

Patient	Age	Sex	KCS	Xerostomia	Rheumatoid Arthritis	Salivary Gland Enlargement	Associated Disease
A1	63	F	+	+	+	-	
A2	54	M	+	+	+	-	Simple Goitre.
A3	56	F	+	+	+	-	Primary Hypothyroidism
A4	78	F	+	+	+	+	Myasthenia Gravis
A5	59	F	+	+	+	-	
A6	65	F	+	+	+	-	
A7	53	M	+	+	+	-	
A8	58	F	+	+	+	-	Thrombophlebitis
A9	47	F	-	+	+	-	Hashimoto's Thyroiditis
A10	67	F	+	+	+	-	
A11	78	F	+	+	+	-	Iron Def. Anaemia
A12	54	F	+	+	+	-	
B1	62	M	+	+	-	-	
B2	66	F	+	+	-	-	
B3	53	F	+	+	-	-	Anaemia
B4	73	F	+	+	-	-	Raynaud's Phenomenon
B5	63	F	+	+	-	-	
B6	59	M	+	+	-	-	
B7	54	F	+	+	-	+	
B8	64	F	+	+	-	-	
B9	55	F	+	+	-	-	
B10	56	F	+	+	-	+	
B11	73	F	+	+	-	-	Simple Goitre
B12	65	F	+	+	-	+	Pernicious Anaemia Hashimoto's Thyroiditis
B13	72	F	+	+	-	-	Hashimoto's Thyroiditis
B14	61	F	+	+	-	-	
B15	67	F	+	+	-	-	
B16	72	F	+	+	-	-	Raynaud's Phenomenon
B17	54	F	+	+	-	-	
B18	53	F	+	+	-	-	Thyrotoxicosis Raynaud's Phenomenon

TABLE IV, 3

LABORATORY DETAILS IN THE 30 PATIENTS STUDIED

Patient	W.B.C. /cmm.	E.S.R. (mm. in 1st hr.)	H.b. (g/100 ml)	Globulins (g/100 ml)	S.S.C.A. Test [1]	Hyland R.A.	L.E. Test		A.N.F. Test [2]	Non-organ specific prec. test [3]	T.T.R.C. Test [4]
							Cells	Latex			
A1	5,200	70	13.3	2.6	+	+	-	-	+(1000H)	-	-
A2	5,200	40	15.4	3.8	-	+	-	-	+(16H)	-	-
A3	3,400	20	13.3	4.3	+ve (128)	+	-	-	+(1000S)	+	+(4000)
A4	6,000	15	11.8	2.2	+ve (64)	+	-	-	+(16S)	-	+(4000)
A5	5,650	21	13.3	3.0	+ve (128)	+	-	-	+(16H)	-	
A6	7,700	32	11.8	2.9	+ve (128)	+	-	-	+(64H)	+	-
A7	7,600	108	11.3	4.5	+(512)	+	-	-	-	-	-
A8	6,150	12	11.9	3.1	+(512)	+	-	-	+(16H)	-	-
A9	5,200	70	12.3	3.8	+(2048)	+	-	-	-	+	+(4000)
A10	4,000	62	13.4	4.1	+(512)	+	-	-	+(16H)	-	-
A11	7,600	119	9.7	4.2	+(1024)	+	-	-	+(64H)	+	-
A12	7,900	64	12.4	3.5	+(128)	+	-	-	+(256H)	+	-
B1	5,000	32	14.1	3.6	+(128)	+	-	-	+(1000H)	-	+(4000)
B2	3,900	38	12.6	4.2	-	+	-	-	-	-	-
B3	9,700	80	8.0	2.1	-	-	-	-	+(16H)	-	-
B4	6,300	16	13.0	2.0	+(64)	+	-	-	+(64H)	-	-
B5	3,300	25	12.7	2.9	-	+	-	-	-	-	-
B6	12,600	41	16.1	3.8	-	+	-	-	-	-	-
B7	4,500	10	15.0	3.5	-	+	-	-	-	-	+(256)
B8	7,200	20	13.2	3.4	-	-	-	-	-	-	-
B9	3,900	21	15.3	2.9	-	-	-	-	-	-	-
B10	6,900	14	13.8	3.3	+(128)	+	-	-	-	-	-
B11	4,900	34	10.6	3.2	+(128)	+	-	-	+(16H)	-	-
B12	2,500	26	8.2	3.1	-	+	-	-	-	+	-
B13	5,000	45	12.7	4.3	-	-	-	-	-	+	+(4000)
B14	6,800	26	13.1	3.3	+(128)	+	-	-	-	-	-
B15	-	11	14.8	2.9	-	-	-	-	+(16H)	-	-
B16	6,950	14	13.3	3.3	-	-	-	-	-	-	-
B17	6,100	8	10.3	3.3	-	+	-	-	+(16H)	+	-
B18	9,700	10	15.7	-	-	+	-	-	-	-	-

(The numbers bracketed are the reciprocal of the titre)

1. SSCA = Sensitised sheep cell agglutination test for rheumatoid factor, starting titre 1:32,
2. ANF = antinuclear factor H = homogenous staining S = speckled staining N = nucleolar staining, starting titre 1:16,
3. Precipating auto-antibodies to tissue components, undiluted serum,
4. TTRC Test = thyroglobulin tanned red cell test, starting titre 1:16.

TABLE IV; 4

CLINICAL DETAILS OF THE PATIENTS STUDIED - ORAL SYMPTOMS ASSOCIATED WITH XEROSTOMIA

Patient	Oral Dryness			Difficulty with Mastication	Difficulty with Swallowing	Increased Fluid Intake		Taste Abnormal	Oral Soreness	Ill-fitt. dentures	Oral Ulceration	Fissuring or Ulceration of lips
	Duration	Intermittent	Persistent			With Meals	In General					
A1	25	-	x	x	x	x	-	-	x	x	-	x
A2	7	x	-	x	-	x	x	-	x	x	-	x
A3	8	x	-	x	-	x	-	-	x	-	-	x
A4	22	-	x	x	x	x	x (N)	x	x	x	-	x
A5	1	x	-	x	-	x	x (N)	-	x	x	x (T)	x
A6	6	-	x	x	-	x	x (N)	-	-	-	-	-
A7	2½	x	-	x	-	-	-	-	-	-	-	x
A8	8	x	-	-	-	-	x	-	x	-	x (A)	x
A9	16	x	-	-	-	x	x	-	-	-	x (T)	-
A10	1	x	-	-	-	-	x	-	-	-	-	-
A11	2	x	-	-	-	-	-	-	-	x	x (T)	-
A12	1	-	x	x	-	x	x	-	x	x	-	x
B1	12	-	x	x	-	x	x (N)	-	-	x	-	x
B2	5	x	-	-	-	x	x	-	-	-	-	-
B3	1	x	-	x	-	-	x	-	x	-	-	x
B4	4	-	x	x	-	x	x (N)	-	x	x	-	x
B5	10	x	-	-	-	x	x (N)	-	-	-	x (A)	-
B6	1	x	-	-	-	-	x	-	-	-	-	-
B7	5	x	-	-	-	-	-	-	-	-	-	-
B8	3	x	-	x	-	x	x	-	-	x	-	x
B9	2	-	x	x	-	x	x	-	x	x	x (T)	x
B10	7	-	x	x	-	x	-	x	-	x	-	x
B11	4	x	-	x	-	x	x	-	-	-	-	x
B12	2	-	x	-	-	-	x (N)	-	-	x	-	-
B13	2	-	x	-	-	-	x (N)	-	-	x	-	x
B14	3	-	x	x	-	x	x	-	x	x	-	x
B15	1	x	-	-	-	-	-	-	x	-	-	-
B16	5	x	-	-	-	-	-	-	x	-	-	-
B17	3	-	x	x	x	x	x (N)	-	x	x	-	x
B18	5	x	-	-	x	-	x	-	-	-	-	-

(N) - Increased Fluid Intake at Night (T) - Traumatic Ulcer (A) - Aphthous Ulcer

TABLE IV, 5

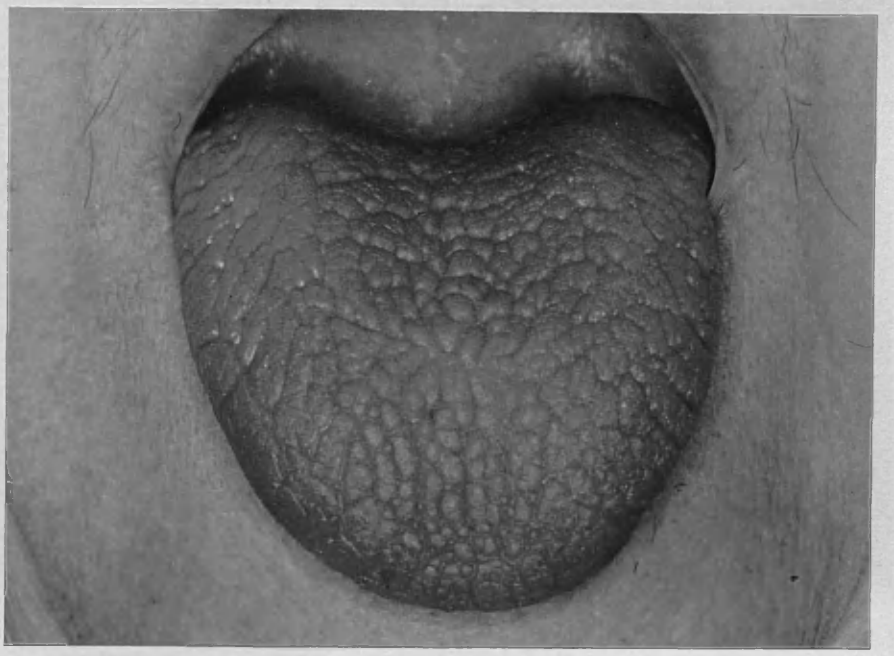
CLINICAL DETAILS OF THE PATIENTS STUDIED

ORAL SIGNS ASSOCIATED WITH XEROSTOMIA

Patient	Dry Mouth	Tongue Fissured	Angular Cheilitis or Cheilosis	Ulceration
A1	X	X	–	–
A2	X	X	X	–
A3	X	X	X	–
A4	X	X	X	–
A5	X	–	–	–
A6	X	X	–	–
A7	X	–	X	–
A8	–	X	–	X (A)
A9	–	–	X	–
A10	–	–	–	–
A11	–	–	–	–
A12	X	X	X	–
B1	X	X	X	–
B2	X	–	–	–
B3	X	X	X	–
B4	X	X	X	–
B5	X	–	–	X (A)
B6	–	–	–	–
B7	–	–	–	–
B8	X	X	–	–
B9	X	X	–	X (T)
B10	X	X	–	–
B11	X	–	–	–
B12	–	–	–	–
B13	–	–	–	–
B14	X	–	–	–
B15	–	–	–	–
B16	–	–	–	–
B17	X	X	X	–
B18	–	–	–	–

(A)= Aphthous **(T)= Traumatic**

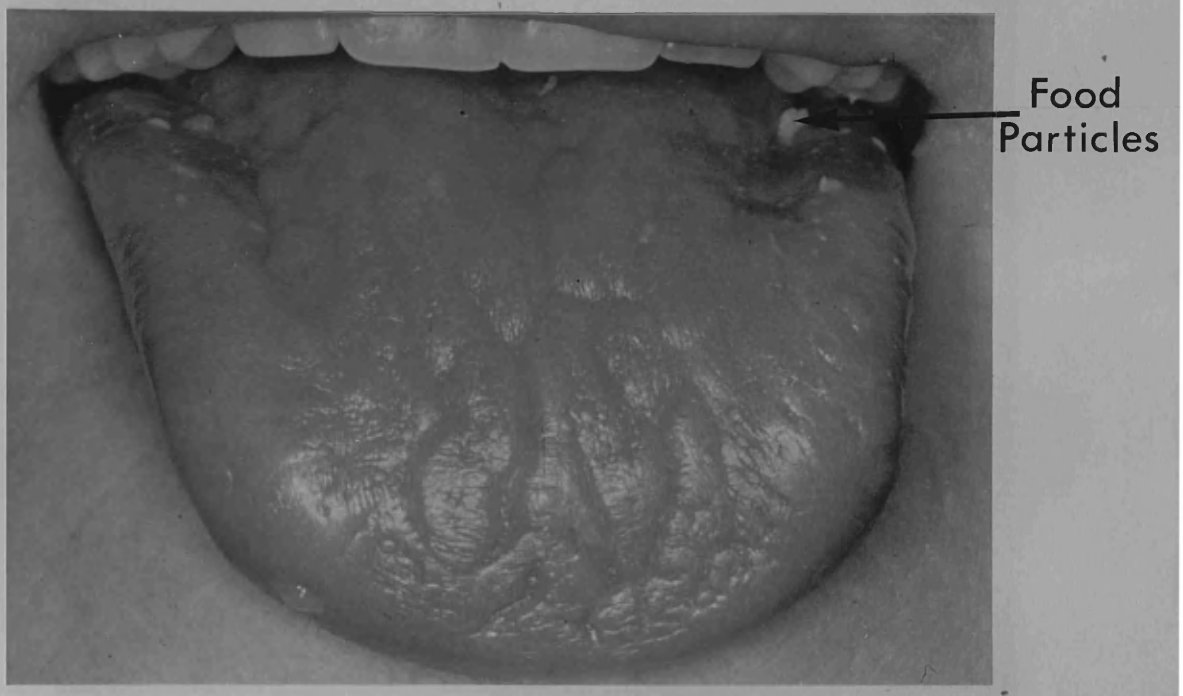
FIGURE IV, 3



SJÖGREN'S SYNDROME

Extreme oral dryness, atrophic mucosa and fissuring of tongue in Sjögren's syndrome and xerostomia of 22 yrs. duration. (Patient A4).

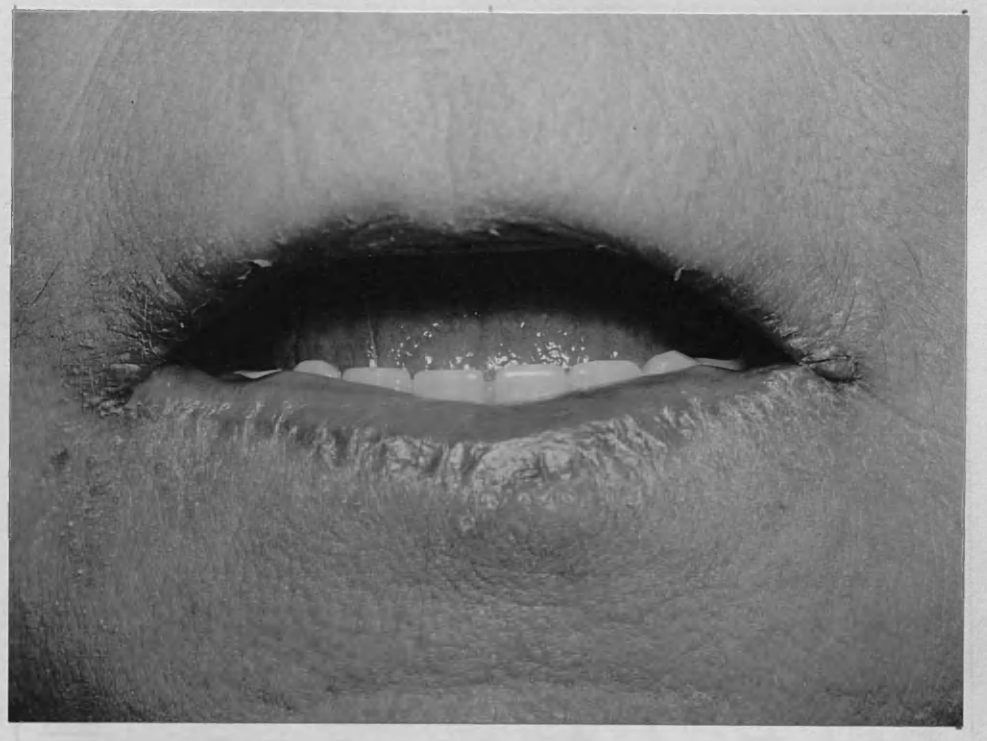
FIGURE IV, 4



SJÖGREN'S SYNDROME

Fissured dry tongue with food particles sticking to the surface in a patient (A1) with Sjögren's syndrome.

FIGURE IV, 5



SJÖGREN'S SYNDROME

Dry lips with angular cheilosis in a patient with Sjögren's syndrome and xerostomia of 8 yrs. duration. (Patient B10).

TABLE IV, 6

SYMPTOMS AND SIGNS ASSOCIATED WITH XEROSTOMIA

		GROUP 'A'	GROUP 'B'	TOTAL
Number of Patients		12 (100%)	18 (100%)	30 (100%)
Mean Duration of Xerostomia (yrs)		7.9	4.1	5.9
SYMPTOMS -	Oral Dryness	12 (100%)	18 (100%)	30 (100%)
	" " Intermittent	8 (67%)	10 (55%)	18 (60%)
	" " Persistent	4 (33%)	8 (44%)	12 (40%)
	Difficulty in Mastication	8 (66%)	9 (50%)	17 (57%)
	Difficulty in Swallowing	2 (17%)	2 (11%)	4 (13%)
	Increased Fluid Intake - with meals	8 (67%)	10 (56%)	18 (60%)
	- in general	8 (67%)	14 (78%)	22 (73%)
	- during night	3 (25%)	5 (28%)	8 (27%)
	Abnormalities of Taste	1 (8%)	1 (6%)	2 (7%)
	Oral Soreness	5 (42%)	8 (44%)	13 (43%)
	Ill fitting dentures	5 (42%)	9 (50%)	14 (47%)
	Oral Ulceration	3 (25%)	2 (11%)	5 (17%)
	Fissuring & Ulceration of Lips	6 (50%)	11 (61%)	17 (57%)
SIGNS -	Dry Mouth on Examination	8 (67%)	11 (61%)	19 (63%)
	Fissured tongue	7 (58%)	7 (39%)	14 (47%)
	Fissuring or Ulceration of Lips	5 (42%)	4 (22%)	9 (30%)
	Ulceration of Oral Mucosa	1 (8%)	2 (11%)	3 (10%)

TABLE IV, 7

COMPARISON OF ORAL SYMPTOMS AND SIGNS IN PATIENTS WITH NORMAL AND ABNORMAL SIALOGRAMS

		Normal Sialogram	Abnormal Sialogram
Number of Patients		14 (100%)	16 (100%)
Mean Duration of Xerostomia (yrs)		3.1	8.1
SYMPTOMS -	Oral Dryness	14 (100%)	16 (100%)
	" " Intermittent	11 (79%)	7 (44%)
	" " Persistent	3 (21%)	9 (56%)
	Difficulty in Mastication	5 (36%)	12 (75%)
	Difficulty in Swallowing	1 (7%)	3 (19%)
	Increased Fluid Intake - with meals	4 (29%)	14 (88%)
	- in general	11 (79%)	11 (69%)
	- during night	2 (14%)	6 (38%)
	Abnormalities of Taste	0 (0%)	2 (13%)
	Oral Soreness	3 (21%)	10 (63%)
	Ill Fitting Dentures	5 (36%)	9 (56%)
	Oral Ulceration	2 (14%)	3 (19%)
	Fissuring or Ulceration of Lips	4 (29%)	13 (81%)
SIGNS -	Dry Mouth on Examination	5 (36%)	14 (88%)
	Fissured Tongue	2 (14%)	12 (75%)
	Fissuring or Ulceration of Lips	1 (7%)	8 (50%)
	Ulceration of Oral Mucosa	1 (7%)	2 (13%)

TABLE IV, 8

SIALOGRAPHIC FINDINGS IN GROUPS A & B

GROUP 'A'

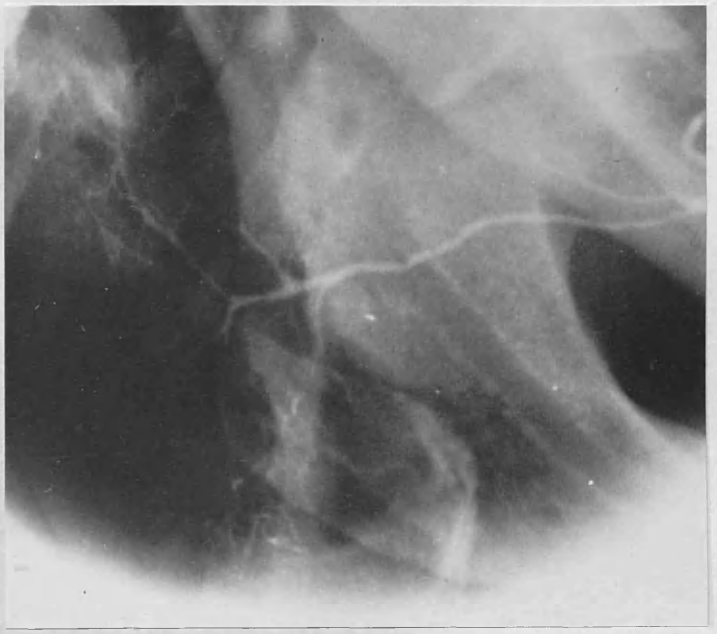
Patient	NORMAL	ATROPHIC	SIALECTASIS		
			Punctate	Globular	Cavitary
A1	o	x	o	o	o
A2	o	x	x	o	o
A3	o	x	x	o	o
A4	o	x	o	o	x
A5	x	o	o	o	o
A6	o	o	o	x	o
A7	x	o	o	o	o
A8	x	o	o	o	o
A9	o	o	o	x	o
A10	x	o	o	o	o
A11	x	o	o	o	o
A12	o	x	o	o	o

GROUP 'B'

Patient	NORMAL	ATROPHIC	SIALECTASIS		
			Punctate	Globular	Cavitary
B1	o	x	o	x	o
B2	o	x	o	o	x
B3	o	o	x	o	o
B4	o	x	o	o	x
B5	o	o	x	o	o
B6	x	o	o	o	o
B7	x	o	o	o	o
B8	x	o	o	o	o
B9	o	x	o	o	o
B10	o	o	x	o	o
B11	x	o	o	o	o
B12	x	o	o	o	o
B13	x	o	o	o	o
B14	x	o	o	o	o
B15	o	o	x	o	o
B16	x	o	o	o	o
B17	o	x	o	x	o
B18	x	o	o	o	o

FIGURE IV, 6

(A)



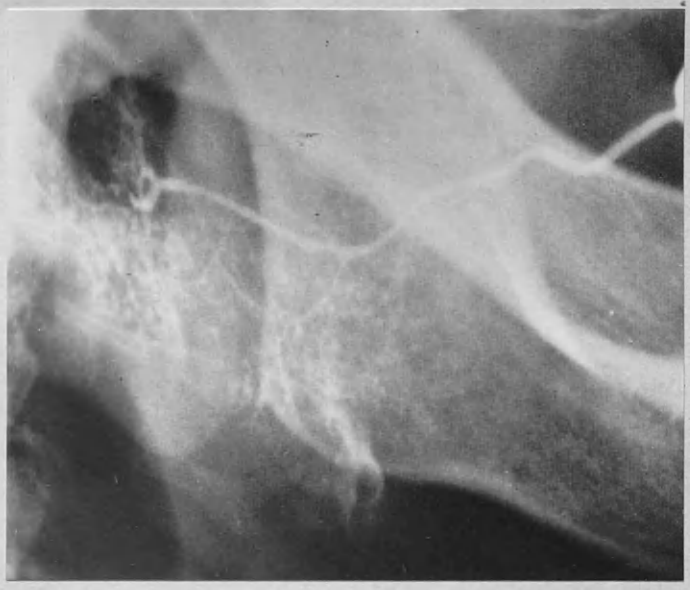
(B)

SJÖGREN'S SYNDROME - PAROTID GLAND ATROPHY

Sialographic comparison of atrophic gland in Sjögren's syndrome (A) with normal gland (B) - Lateral Oblique View.

FIGURE IV, 7

(A)



(B)

SJÖGREN'S SYNDROME - PUNCTATE SIALECTASIS

Sialographic examples of (A) normal gland and (B) punctate sialectasis in Sjögren's syndrome.

FIGURE IV, 8

(A)

(B)

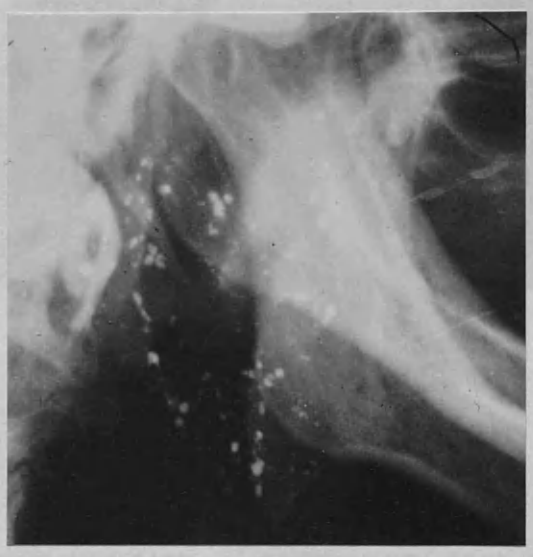
SJÖGREN'S SYNDROME - PUNCTATE SIALECTASIS

Sialograms of (A) normal gland and (B) punctate sialectasis in Sjögren's syndrome (antero-posterior view).

FIGURE IV , 9

(A)

(B)



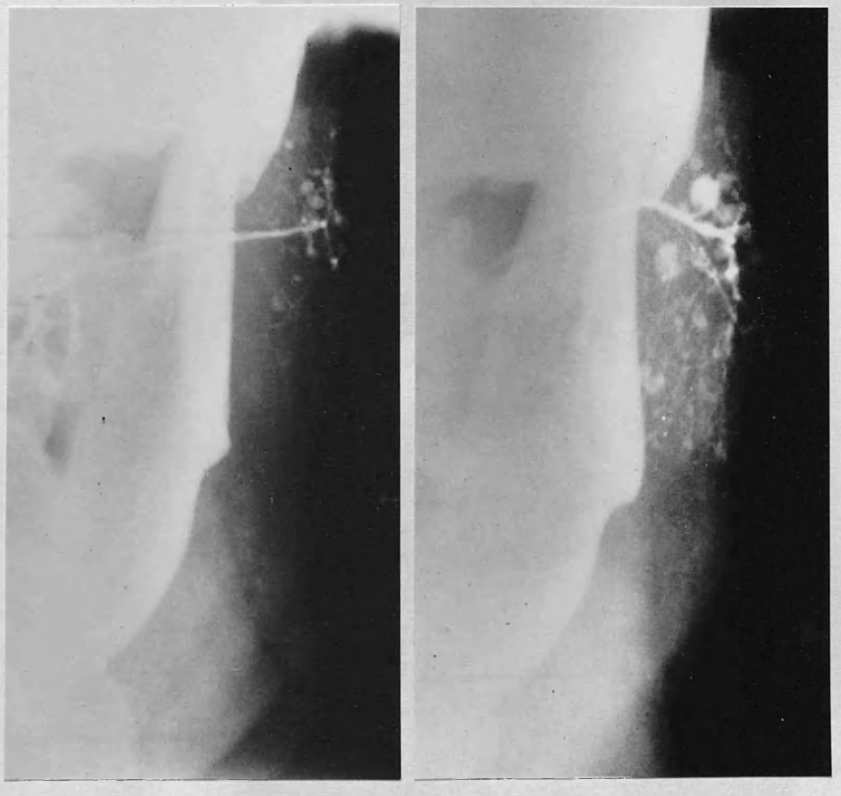
SJÖGREN'S SYNDROME - RETENTION OF CONTRAST MEDIUM

Sialograms typical of Sjögren's syndrome.
There is prolonged retention of contrast medium within gland and ducts in (B).

(A) Filling Phase (B) Secretory Phase

FIGURE IV, 10

(A)



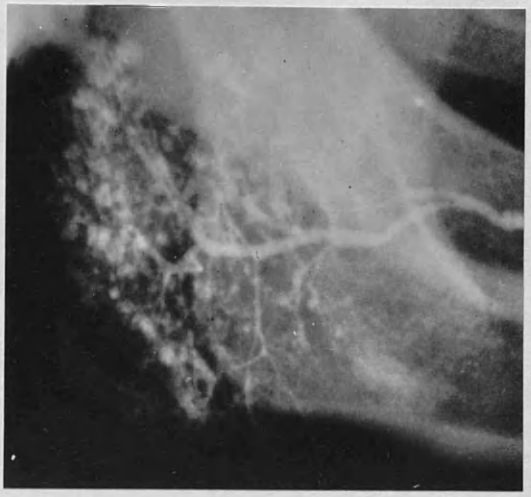
(B)

SJÖGREN'S SYNDROME - GLOBULAR AND CAVITARY SIALECTASIS

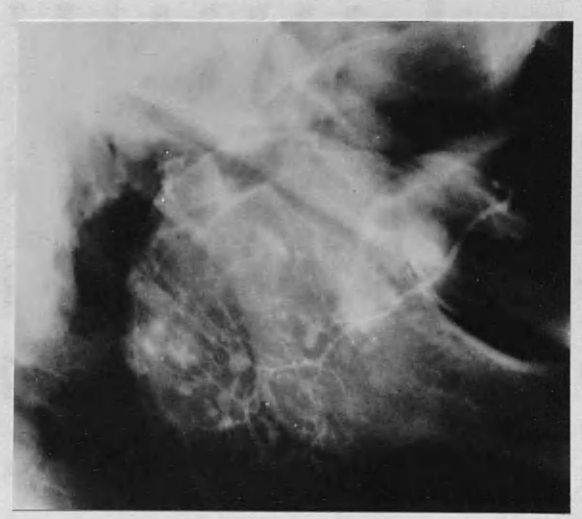
Sialographic examples of (A) globular and (B) cavitary sialectasis in Sjögren's syndrome (antero-posterior view).

FIGURE IV, 11

(A)



(B)



SJÖGREN'S SYNDROME - GLOBULAR AND CAVITARY SIALECTASIS

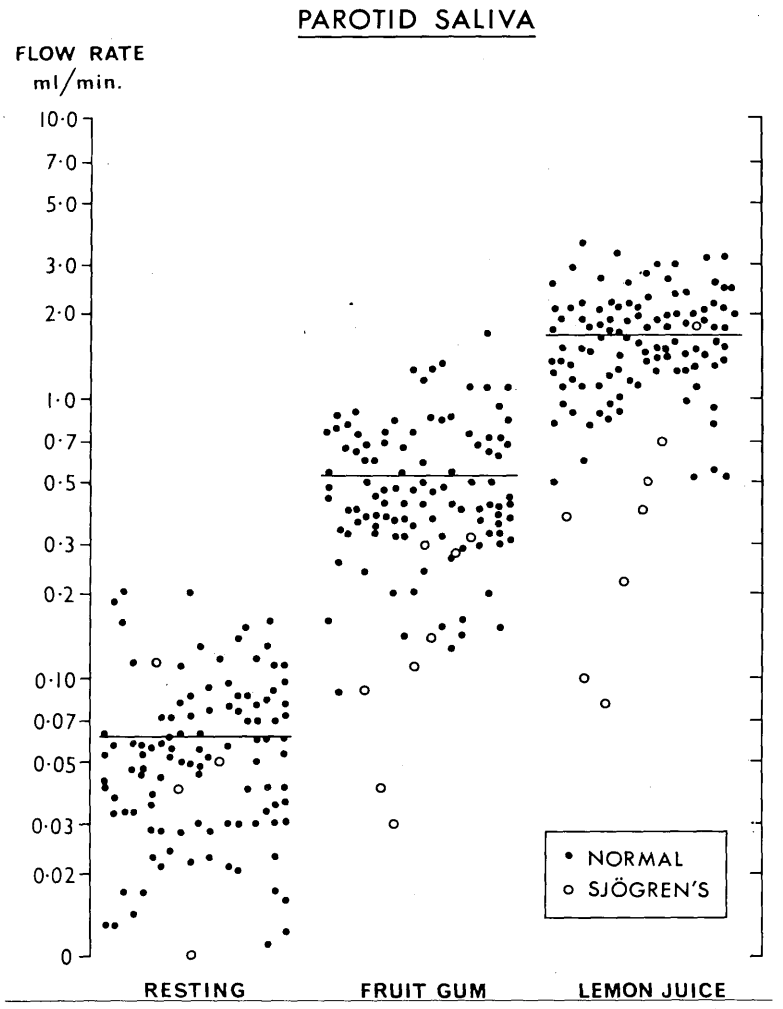
Sialographic appearances of (A) globular and (B) cavitary sialectasis (lateral oblique views)

TABLE IV, 9

PAROTID SALIVARY FLOW RATES (ml/min) IN GROUP 'A', 'B' AND A CONTROL GROUP 'C'

GROUP 'A'						GROUP 'B'						GROUP 'C'					
PATIENT	AGE	SEX	'RESTING'	FRUIT GUM	LEMON JUICE	PATIENT	AGE	SEX	'RESTING'	FRUIT GUM	LEMON JUICE	SUBJECT	AGE	SEX	'RESTING'	FRUIT GUM	LEMON JUICE
(S) A1	63	F	0 *	0	0 *	(S)B1	62	M	0 *	0.09	0.38 *	C1	48	M	0.05	0.68	1.80
(S) A2	54	M	0 *	0.04 *	0.10 *	(S)B2	66	F	0 *	0.03 *	0.08 *	C2	75	M	0.05	0.38	1.65
(S) A3	56	F	0.04	0.11	0.22 *	(S)B3	53	F	0.001 *	0.14	0.40 *	C3	67	F	0.04	0.54	1.35
(S) A4	78	F	0 *	0 *	0 *	(S)B4	73	F	0 *	0 *	0 *	C4	52	F	0.03	0.34	1.30
A5	59	F	0.08	0.41	0.78	(S)B5	63	F	0	0.28	0.70	C5	58	F	0.03	0.87	1.10
A7	53	M	0.03	0.39	1.90	B6	59	M	0.04	0.48	2.10	C6	48	F	0.02	0.35	2.22
A8	58	F	0.14	1.18	1.03	B7	54	F	0.05	0.30	1.30	C7	53	F	0.03	0.60	1.76
(S) A9	48	F	0.12	0.30	1.85	B8	64	F	0.14	0.53	1.50	C8	62	F	0.03	0.69	0.93
A10	67	F	0.04	0.39	0.95	B11	73	F	0.07	0.31	1.40	C9	67	F	0.06	0.83	1.88
(S)A12	54	F	0.05	0.32	0.50	B12	65	F	0.13	0.50	0.75	C10	70	F	0.03	0.42	1.16
						B16	72	F	0.10	0.63	2.50	C11	64	F	0.09	0.47	0.97
						(S)B17	54	F	0 *	0 *	0 *	C12	51	F	0.13	0.38	3.03
						B18	53	F	0 *	0.19	0.68	C13	62	F	0.02	0.20	0.89
RANGE	48-78		0-0.14	0-1.18	0-1.90	RANGE	53-73		0-0.14	0-0.53	0-2.50	RANGE	48-75		0.02-0.13	0.20-0.87	0.89-3.03
MEAN	59.00		0.05	0.31	0.73	MEAN	62-40		0.04	0.27	0.90	MEAN	59.77		0.05	0.52	1.54

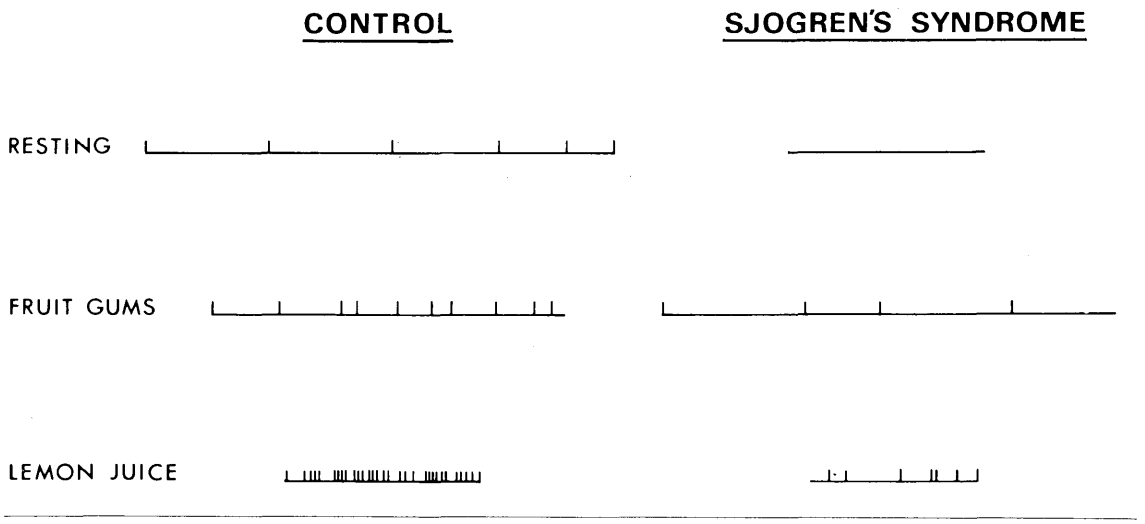
FIGURE IV, 12



SJÖGREN'S SYNDROME - SALIVARY FLOW RATES IN 12 PATIENTS WITH ABNORMAL SIALOGRAMS COMPARED WITH 93 NORMAL SUBJECTS

No saliva was obtained from - 8 patients under resting conditions
No saliva was obtained from - 4 patients after stimulation.

FIGURE IV, 13



PAROTID SALIVA DROP RATE IN SJÖGREN'S SYNDROME

Tracings from photoelectric drop counter showing reduced salivary flow rate in patient (A.2) with Sjögren's Syndrome compared with control under resting conditions and after fruit gum and lemon juice stimulation.

TABLE IV, 10

COMPARISON OF PAROTID SALIVARY FLOW RATES IN 10 PATIENTS WITH NORMAL AND ABNORMAL SIALOGRAMS AND CONTROL NORMAL GROUP. PAROTID SALIVA (ml/min) UNDER 'RESTING' CONDITIONS, AND AFTER FRUIT GUM AND LEMON JUICE STIMULATION.

NORMAL SIALOGRAMS						ABNORMAL SIALOGRAMS						CONTROL GROUP					
PATIENT	AGE	SEX	'RESTING'	FRUIT GUM	LEMON JUICE	PATIENT	AGE	SEX	'RESTING'	FRUIT GUM	LEMON JUICE	SUBJECT	AGE	SEX	'RESTING'	FRUIT GUM	LEMON JUICE
B6	59	M	0.04	0.48	2.10	B1	62	M	0 *	0.09	0.38 *	C1	48	M	0.05	0.68	1.80
B7	54	F	0.05	0.30	1.30	A2	54	M	0 *	0.04 *	0.10 *	C2	75	M	0.05	0.38	1.65
B8	64	F	0.14	0.53	1.50	B2	66	F	0 *	0.03 *	0.08 *	C3	67	F	0.04	0.54	1.35
A5	59	F	0.08	0.41	0.78	A3	56	F	0.04	0.11	0.22 *	C4	52	F	0.03	0.34	1.30
A7	53	M	0.03	0.39	1.9	B3	53	F	0.001 *	0.14	0.40 *	C5	58	F	0.03	0.87	1.10
B11	73	F	0.31	0.31	1.40	A4	78	F	0 *	0 *	0 *	C6	48	F	0.02	0.35	2.22
B12	65	F	0.13	0.50	0.75	B4	73	F	0 *	0 *	0 *	C7	53	F	0.03	0.60	1.76
A8	72	F	0.14	1.18	1.03	B5	63	F	0 *	0.28	0.70	C8	62	F	0.03	0.69	0.93
B16	72	F	0.11	0.63	2.50	A12	54	F	0.05	0.32	0.50	C9	67	F	0.06	0.83	1.88
B18	53	F	0 *	0.19	0.68	B17	54	F	0 *	0 *	0 *	C10	70	F	0.03	0.42	1.16
RANGE	53-73	-	0-0.31	0.19-1.18	0.68-2.50	RANGE	53-78	-	0-0.05	0-0.32	0-0.70	RANGE	48-75	-	0.02-0.06	0.34-0.87	0.93-1.88
MEAN	62.40	-	0.10	0.49	1.39	MEAN	61.30	-	0.009	0.10	0.24	MEAN	60.00	-	0.04	0.57	1.52
S.E.M.	2.33	-	.031	0.103	0.185	S.E.M	2.70	-	-	0.013	0.075	S.E.M	3.05	-	.003	.054	0.329

* Below normal range

0 = No saliva obtained

FIGURE IV, 14

(A)

(B)

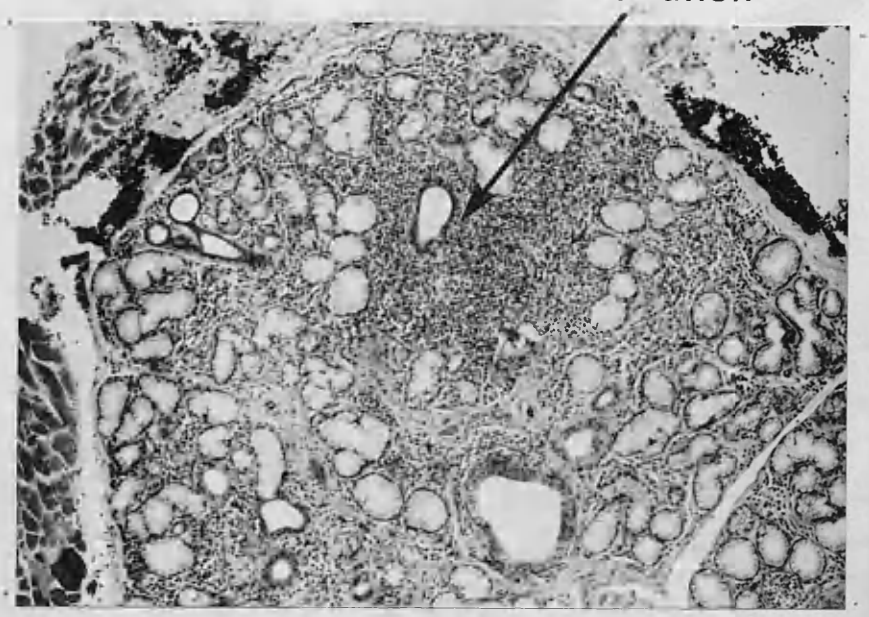
SJÖGREN'S SYNDROME - COMPARISON OF SIALOGRAPHIC APPEARANCES USING HAND INJECTION TECHNIQUE AND HYDROSTATIC METHOD.

(A) Hand injection method - where overfilling has occurred and typical Sjögren's features are masked

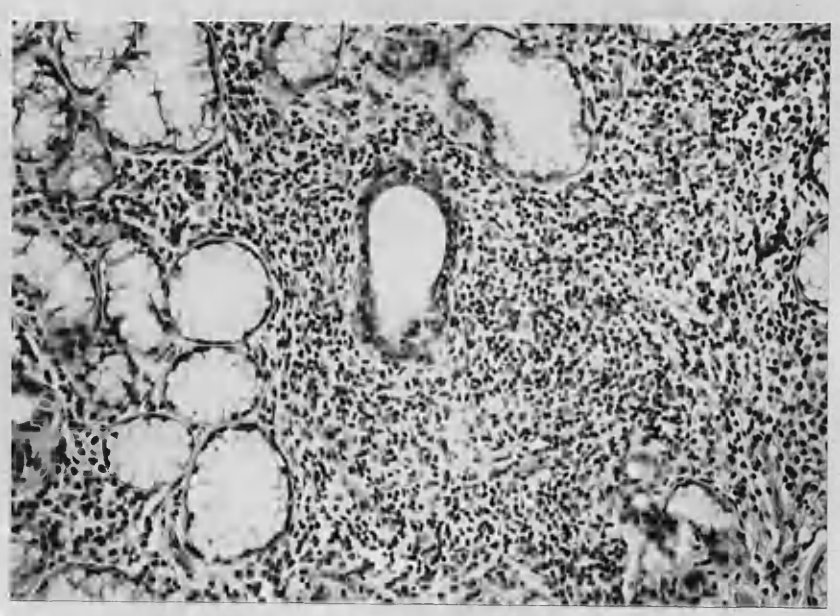
(B) Hydrostatic method and same patient - punctate sialectasis is now apparent.

FIGURE IV, 15

(A)



(B)



LABIAL MUCOUS GLANDS IN A PATIENT (B5) WITH SJÖGREN'S SYNDROME

There is Lymphocytic Infiltration with Acinar Atrophy.

(A) Magnification x 75
(B) Magnification x 190

TABLE IV, 11

GROUP (1) - SJÖGREN'S SYNDROME

PATIENT	AGE	SEX	HISTO PATHOLOGY[1]	SEROLOGY						SIALO-GRAPHY	SAL. FLOW DECREASED (PAROTID)
				L.E. CELL TEST	S.S.C.A. TEST[2]	HYLAND R.A. TEST	A.N.F. TEST[3]	NON-ORGAN SPECIFIC PREC. TEST[4]	T.T.R.C. TEST[5]		
A2	54	M	+	-	-	+	+ (16H)	-	-	+	+
A3	56	F	++	-	+ (128)	+	+ (1000S)	+	+ (4000)	+	+
A5	59	F	+	-	+	+	+ (16H)	-	-	-	-
A12	54	F	++	-	+ (128)	+	+ (256H)	+	-	+	-
B1	62	M	-	-	+ (128)	+	+ (1000H)	-	+ (4000)	+	+
B2	66	F	++	-	-	+	-	-	-	+	+
B5	63	F	+	-	-	+	-	-	-	+	-
B10	56	F	++	-	+ (128)	+	-	-	-	+	+

(The numbers in brackets are the reciprocal of the titre)

1. HISTOPATHOLOGICAL APPEARANCES
   + = 1 or more foci of lymphocytes containing at least 50 cells
   ++ = 3 or more " " " " " " " "
   - = ———no " " " " " " " "

2. S.S.C.A. = sensitised sheep cell agglutination test for rheumatoid factor, starting titre 1:32

3. A.N.F. = antinuclear factor H = homogenous staining S = speckled staining, starting titre 1:16

4. Precipitating auto-antibodies to tissue components, undiluted serum

5. T.T.R.C. Test = thyroglobulin tanned red cell test, starting titre 1:16

TABLE IV, 12

GROUP (2) - RHEUMATOID ARTHRITIS

PATIENT	AGE	SEX	HISTO PATHOLOGY[1]	SEROLOGY					
				L.E. CELL TEST	S.S.C.A. TEST[2]	HYLAND R.A. TEST	A.N.F. TEST[3]	NON-ORGAN SPECIFIC PREC. TEST[4]	T.T.R.C. TEST[5]
R1	50	F	+	-	-	+	-	-	+(16)
R2	43	M	-	-	+(572)	+	-	-	-
R3	59	F	+	-	+(128)	+	-	-	-
R4	60	M	+	-	+(128)	+	-	-	-
R5	59	F	-	-	+(32)	+	N.D. *	N.D. *	N.D. *
R6	45	F	+	-	+(64)	+	+(1000H)	-	+(64)
R7	62	F	-	-	+(128)	+	-	-	-
R8	67	F	-	-	+(256)	+	-	-	-

(The numbers in brackets are the reciprocal of the titre) * N.D. Not done

1. HISTOPATHOLOGICAL APPEARANCES
   + = 1 or more foci of lymphocytes containing at least 50 cells
   ++ = 3 or more " " " " " " " "
   - = ———no " " " " " " " "
2. S.S.C.A.= sensitised sheep cell agglutination test for rheumatoid factor, starting titre 1:32
3. A.N.F. = antinuclear factor H = homogenous staining S = speckled staining, starting titre 1:16
4. Precipitating auto-antibodies to tissue components, undiluted serum
5. T.T.R.C.Test = thyroglobulin tanned red cell test, starting titre 1:16

TABLE IV, 13

GROUP (3) - CONTROLS

PATIENT	AGE	SEX	HISTO PATHOLOGY[1]	SEROLOGY					
				L.E. CELL TEST	S.S.C.A. TEST[2]	HYLAND R.A. TEST	A.N.F. TEST[3]	NON-ORGAN SPECIFIC PREC. TEST[4]	T.T.R.C. TEST[5]
C1	79	F	-	-	-	-	-	-	-
C2	55	F	-	-	+ (32)	+	-	-	-
C3	33	F	-	-	+ (128)	+	-	-	-
C4	53	F	-	-	N.D. *	N.D. *	-	-	-
C5	66	M	-	-	-	-	-	-	-
C6	42	M	-	-	-	-	-	-	-
C7	56	F	-	-	+ (128)	+	+ (64H)	-	-
C8	54	F	-	-	-	-	-	-	-

(The numbers in brackets are the reciprocal of the titre) * N.D. Not done

1. HISTOPATHOLOGICAL APPEARANCES
   + = 1 or more foci of lymphocytes containing at least 50 cells
   ++ = 3 or more " " " " " " " "
   - = ------no " " " " " " " "
2. S.S.C.A. = sensitised sheep cell agglutination test for rheumatoid factor, starting titre 1:32
3. A.N.F. = antinuclear factor H = homogenous staining S = speckled staining, starting titre 1:16
4. Precipitating auto-antibodies to tissue components, undiluted serum
5. T.T.R.C. Test = thyroglobulin tanned red cell test, starting titre 1:16

TABLE IV, 14

RESULTS of SIALOGRAPHY in HASHIMOTO'S THYROIDITIS, PRIMARY HYPOTHYROIDISM, and HOSPITAL 'CONTROLS'.

Clinical Group	No.	Age in Years		Sialographic Abnormalities					
		Mean	Range	No. Abnormal	Punctate	Punctate with intermediate duct changes	Globular	No. with abnormal sialograms and xerostomia	No. with abnormal sialograms and salivary gland enlargement
Hashimoto's Thyroiditis	41	53.2	37-72	7 (17%)	3	2	2	6	0
Primary Hypothyroidism	32	67.0	33-74	5 (16%)	3	2	0	4	0
Hospital Controls	36	51.0	42-74	6 (17%)	4	2	0	6	0

TABLE IV, 15

KERATOCONJUNCTIVITIS SICCA IN THYROID DISEASE

Clinical Groups	Number	Age in Years		Keratoconjunctivitis Sicca
		Mean	Range	
Hashimoto's Thyroiditis	41	53.2	37-72	2 (4.9%)
Primary Hypothyroidism	32	67.0	33-74	2 (6.3%)
Hospital Controls	36	51.0	42-74	2 (5.5%)